PB81-117301

Ambient Water Quality Criteria for Aldrin/Dieldrin

(U.S.) Environmental Protection Agency
Washington, DC

Oct 30

U.S. Department of Commerce
National Technical Information Service
NTIS

United States
Environmental Protection
Agency

Office of Water
Regulations and Standards
Criteria and Standards Division
Washington DC 20460

EPA 440/5-80-019
October 1980

PB81-117301

EPA

Ambient Water Quality Criteria for Aldrin/Dieldrin

REPRODUCED BY
NATIONAL TECHNICAL
INFORMATION SERVICE
U.S. DEPARTMENT OF COMMERCE
SPRINGFIELD, VA 22161

TECHNICAL REPORT DATA
(Please read Instructions on the reverse before completing)

1. REPORT NO.	2.	3. RECIPIENT'S ACCESSION NO. PB81 117301
4. TITLE AND SUBTITLE Ambient Water Quality Criteria for: Aldrin/Dieldrin		5. REPORT DATE October, 1980
		6. PERFORMING ORGANIZATION CODE NTISEPAOWP
7. AUTHOR(S) Environmental Criteria and Assessment Office		8. PERFORMING ORGANIZATION REPORT NO. EPA 440/5-80-019
9. PERFORMING ORGANIZATION NAME AND ADDRESS Office of Water Regulations and Standards Criteria and Standards Division U.S. Environmental Protection Agency Washington, D.C. 20460		10. PROGRAM ELEMENT NO.
		11. CONTRACT/GRANT NO.
12. SPONSORING AGENCY NAME AND ADDRESS Same.		13. TYPE OF REPORT AND PERIOD COVERED
		14. SPONSORING AGENCY CODE

15. SUPPLEMENTARY NOTES

Supersedes draft document PB 297 916

16. ABSTRACT

Section 304(A) of the Clean Water Act [33 U.S.C. 1314(A)], requires EPA to publish and periodically update water quality criteria. These criteria are to reflect the latest scientific knowledge on the identifiable effects of pollutants on public health and welfare, aquatic life, and recreation. This report presents water quality criteria for Aldrin/Dieldrin. It presents concentration criteria for the protection of freshwater and saltwater aquatic life. It presents 'safe' concentrations for humans, and in the case of suspect or proven carcinogens, gives various levels of incremental cancer risk. A Section 304(A) water quality criterion is a qualitative or quantitative estimate of the concentration of a water constituent or pollutant in ambient waters which, when not exceeded, will ensure a water quality sufficient to protect a specified water use. Under the Act a criterion is a scientific entity, based solely on data and scientific judgment. It does not reflect considerations of economic or technological feasibility nor is it a water quality standard and in itself has no regulatory effect.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group

18. DISTRIBUTION STATEMENT For Public Release	19. SECURITY CLASS *(This Report)* Unclassified	21. NO. OF PAGES
	20. SECURITY CLASS *(This page)* Unclassified	22. PRICE

EPA Form 2220-1 (9-73)

AMBIENT WATER QUALITY CRITERIA FOR
ALDRIN/DIELDRIN

Prepared By
U.S. ENVIRONMENTAL PROTECTION AGENCY

Office of Water Regulations and Standards
Criteria and Standards Division
Washington, D.C.

Office of Research and Development
Environmental Criteria and Assessment Office
Cincinnati, Ohio

Carcinogen Assessment Group
Washington, D.C.

Environmental Research Laboratories
Corvalis, Oregon
Duluth, Minnesota
Gulf Breeze, Florida
Narragansett, Rhode Island

DISCLAIMER

This report has been reviewed by the Environmental Criteria and Assessment Office, U.S. Environmental Protection Agency, and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

AVAILABILITY NOTICE

This document is available to the public through the National Technical Information Service, (NTIS), Springfield, Virginia 22161.

FOREWORD

Section 304 (a)(1) of the Clean Water Act of 1977 (P.L. 95-217), requires the Administrator of the Environmental Protection Agency to publish criteria for water quality accurately reflecting the latest scientific knowledge on the kind and extent of all identifiable effects on health and welfare which may be expected from the presence of pollutants in any body of water, including ground water. Proposed water quality criteria for the 65 toxic pollutants listed under section 307 (a)(1) of the Clean Water Act were developed and a notice of their availability was published for public comment on March 15, 1979 (44 FR 15926), July 25, 1979 (44 FR 43660), and October 1, 1979 (44 FR 56628). This document is a revision of those proposed criteria based upon a consideration of comments received from other Federal Agencies, State agencies, special interest groups, and individual scientists. The criteria contained in this document replace any previously published EPA criteria for the 65 pollutants. This criterion document is also published in satisifaction of paragraph 11 of the Settlement Agreement in Natural Resources Defense Council, et. al. vs. Train, 8 ERC 2120 (D.D.C. 1976), modified, 12 ERC 1833 (D.D.C. 1979).

The term "water quality criteria" is used in two sections of the Clean Water Act, section 304 (a)(1) and section 303 (c)(2). The term has a different program impact in each section. In section 304, the term represents a non-regulatory, scientific assessment of ecological effects. The criteria presented in this publication are such scientific assessments. Such water quality criteria associated with specific stream uses when adopted as State water quality standards under section 303 become enforceable maximum acceptable levels of a pollutant in ambient waters. The water quality criteria adopted in the State water quality standards could have the same numerical limits as the criteria developed under section 304. However, in many situations States may want to adjust water quality criteria developed under section 304 to reflect local environmental conditions and human exposure patterns before incorporation into water quality standards. It is not until their adoption as part of the State water quality standards that the criteria become regulatory.

Guidelines to assist the States in the modification of criteria presented in this document, in the development of water quality standards, and in other water-related programs of this Agency, are being developed by EPA.

STEVEN SCHATZOW
Deputy Assistant Administrator
Office of Water Regulations and Standards

ACKNOWLEDGEMENTS

Aquatic Life Toxicology:

Charles E. Stephan, ERL-Duluth
U.S. Environmental Protection Agency

David J. Hansen, ERL-Gulf Breeze
U.S. Environmental Protection Agency

Mammalian Toxicology and Human Health Effects:

Thomas Connor (author)
University of Texas Medical Branch

Michael L. Dourson (doc. mgr.)
ECAO-Cin
U.S. Environmental Protection Agency

Karen Blackburn (doc. mgr.), ECAO-Cin
U.S. Environmental Protection Agency

Gordon Chesters
University of Wisconsin

David J. Hansen, ERL-Gulf Breeze
U.S. Environmental Protection Agency

Steven D. Lutkenhoff, ECAO-Cin
U.S. Environmental Protection Agency

David J. McKee, ECAO-RTP
U.S. Environmental Protection Agency

Shane S. Que Hee
University of Cincinnati

Jerry F. Stara, ECAO-Cin
U.S. Environmental Protection Agency

James Barnett
University of Texas Medical Branch

William B. Buck
University of Illinois

Gary Chapman, ERL-Duluth
U.S. Environmental Protection Agency

Patrick Durkin
Syracuse Research Corporation

Alfred Garvin
University of Cincinnati

Fumio Matsamura
University of Michigan

W. Bruce Peirano, HERL
U.S. Environmental Protection Agency

Herbert Schumacher
National Center for Toxicological Res.

Roy E. Albert*
Carcinogen Assessment Group
U.S. Environmental Protection Agency

Technical Support Services Staff: D.J. Reisman, M.A. Garlough, B.L. Zwayer, P.A. Daunt, K.S. Edwards, T.A. Scandura, A.T. Pressley, C.A. Cooper, M.M. Denessen.

Clerical Staff: C.A. Haynes, S.J. Faehr, L.A. Wade, D. Jones, B.J. Bordicks, B.J. Quesnell, C. Russom, R. Rubinstein.

*CAG Participating Members:
Elizabeth L. Anderson, Larry Anderson, Dolph Arnicar, Steven Bayard, David L. Bayliss, Chao W. Chen, John R. Fowle III, Bernard Haberman, Charalingayya Hiremath, Chang S. Lao, Robert McGaughy, Jeffrey Rosenblatt, Dharm V. Singh, and Todd W. Thorslund.

TABLE OF CONTENTS

Page

Criteria Summary

Introduction A-1

Aquatic Life Toxicology B-1
  Introduction B-1
  Effects B-1
    Acute Toxicology B-1
    Chronic Toxicology B-4
    Plant Effects B-6
    Residues B-6
    Miscellaneous B-9
    Summary B-10
  Criteria B-12
  References B-43

Mammalian Toxicology and Human Health Effects C-1
  Introduction C-1
  Exposure C-2
    Ingestion from Water C-3
    Ingestion from Food C-5
    Inhalation C-10
    Dermal C-11
  Pharmacokinetics C-11
    Absorption C-11
    Distribution C-12
    Metabolism C-19
    Excretion C-25
  Effects C-32
    Acute, Subacute, and Chronic Toxicity C-32
    Synergism and/or Antagonism C-35
    Teratogenicity C-36
    Mutagenicity C-38
    Carcinogenicity C-44
  Criterion Formulation C-61
    Existing Guidelines and Standards C-61
    Current Levels of Exposure C-62
    Special Groups at Risk C-62
    Basis and Derivation of Criteria C-63
  References C-66
Appendix C-81

CRITERIA DOCUMENT

ALDRIN-DIELDRIN

CRITERIA

Aquatic Life

Dieldrin

For dieldrin the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.0019 µg/l as a 24-hour average, and the concentration should not exceed 2.5 ug/l at any time.

For dieldrin the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.0019 µg/l as a 24-hour average, and the concentration should not exceed 0.71 µg/l at any time.

Aldrin

For freshwater aquatic life the concentration of aldrin should not exceed 3.0 µg/l at any time. No data are available concerning the chronic toxicity of aldrin to sensitive freshwater aquatic life.

For saltwater aquatic life the concentration of aldrin should not exceed 1.3 µg/l at any time. No data are available concerning the chronic toxicity of aldrin to sensitive saltwater aquatic life.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of aldrin through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6} and 10^{-7}. The corresponding recommended criteria are 0.74 ng/l, 0.074 ng/l, and 0.0074 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 0.79 ng/l, 0.079 ng/l, and 0.0079 ng/l, respectively.

For the maximum protection of human health from the potential carcinogenic effects due to exposure of dieldrin through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6} and 10^{-7}. The corresponding recommended criteria are 0.71 ng/l, 0.071 ng/l, and 0.0071 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 0.76 ng/l, 0.076 ng/l, 0.076 ng/l, and 0.0076 ng/l, respectively.

INTRODUCTION

Aldrin and dieldrin have been two of the most widely used domestic pesticides. They are chlorinated hydrocarbon compounds. Although aldrin is used in greater quantity than dieldrin, aldrin quickly transforms into dieldrin in the environment. Hence, there is concern with both compounds. The primary use of the chemicals in the past was for control of corn pests, although they were also used by the citrus industry. Uses are restricted to those where there is no effluent discharge.

Aldrin use in the United States peaked at 19 million pounds in 1966 but dropped to about 10.5 million pounds in 1970. During that same period dieldrin use decreased from 1 million pounds to about 670,000 pounds. The decreased use has been attributed primarily to increased insect resistance to the two chemicals and to development and availability of substitute materials.

Aldrin and dieldrin have been the subject of litigation bearing upon the contention that these substances cause severe aquatic environmental change and are potential carcinogens. In 1970, the U.S. Department of Agriculture cancelled all registrations of these pesticides based upon a concern to limit dispersal in or on aquatic areas. In 1972, under the authority of the Fungicide, Insecticide, Rodenticide Act as amended by the Federal Pesticide Control Act of 1972, USCS Section 135, et. sec., an EPA order lifted cancellation of all registered aldrin and dieldrin for use in deep ground insertions for termite control, nursery clipping of roots and tops of non-food plants, and mothproofing of woolen textiles and carpets where there is no effluent discharge. In 1974, cancellation proceedings disclosed the severe hazard to human health and suspension of registration of aldrin and dieldrin use was ordered; production was restricted for all pesticide products containing aldrin or dieldrin. However, formulated products containing aldrin and dieldrin are imported from Europe each year solely for subsurface soil injection for termite control. Therefore, limits that protect all receiving water uses must be placed on aldrin and dieldrin. The litigation has produced the evidentiary basis for the Administrator's conclusions that aldrin/dieldrin are carcinogenic in mice and rats, approved the Agency's extrapolation to humans of data derived from tests on animals, and affirmed the conclusions that aldrin and dieldrin pose a substantial risk of cancer to humans, which constitutes an "imminent hazard" to man.

Aldrin and dieldrin are white crystalline substances with aldrin melting at 104°C and dieldrin melting between 176 to 177°C. Both are soluble in organic solvents with dieldrin the least soluble of the two. The chemical name for aldrin is 1, 2, 3, 4, 10, 10-hexachloro-1, 4, 4a, 5, 8, 8a-hexahydro-1, 4: 5, 8-exo-dimethanonaphathalene. The chemical name for dieldrin is 1, 2, 3, 4, 10, 10-hexachloro-6, 7-epoxy-1, 4, 4a, 5, 6, 7, 8, 8a-octahydro-endo, exo-1, 4: 5, 8-dimethanonaphthalene.

Aldrin is metabolically converted to dieldrin. This epoxidation has been shown to occur in several species including mammals and poultry, houseflies, locusts, soil microorganisms, a large number of Lepidoptera species, freshwater fish (Gakstatter, 1968), and a number of freshwater invertebrates including protozoa, coelenterates, worms, arthropods, molluscs, and lobsters. The aldrin molecule is biologically altered in the environment to a more stable and at least equally toxic form, dieldrin. Dieldrin is known to be metabolically degraded as shown by Matsumura and Boush (1967) and Patil, et al. (1972); however, its persistence in the environment is due to its extremely low volatility (i.e., a vapor pressure of 1.78 x 10^{-7} mm mercury at 20°C) and low solubility in water (186 µg/l at 25 to 29°C) (Int. Agency Res. Cancer, 1974). In addition, dieldrin is extremely apolar, resulting in a high affinity for fat which accounts for its retention in animal fats, plant waxes, and other such organic matter in the environment. The fat solubility of dieldrin results in the progressive accumulation in the food chain which may result in a concentration in an organism which would exceed the lethal limit for a consumer.

Many organisms not in direct contact with contaminated water and sediment accumulate aldrin/dieldrin from the food supply. This biological concentration results in tissue concentrations many times those found in the surrounding environment (Sanborn and Yu, 1973). Concentrations increase in the food chain reaching the carnivores at the top including man.

Dieldrin is probably the most stable insecticide among the cyclodienes (i.e., isodrin-endrin; heptaclor-heptachlor epoxide). The time required for 95 percent of the dieldrin to disappear from soil has been estimated to vary from 5 to 25 years depending upon the microbial flora of the soil (Edwards, 1966). Dieldrin applied at 100 ppm has been shown to persist in soil for more than six years (Westlake and San Antonio, 1960), while at 25 ppm in a different soil type, a 50 percent loss was found at seven years (Nash and

Woolson, 1967). When applied to sandy soil at a rate of 100 ppm, residues could be found 15 years later. Matsumura and Boush (1967) found that of 577 bacterial isolates collected from areas heavily contaminated with dieldrin, 10 isolates would alter dieldrin to two to nine unidentified metabolites. The microbes were members of Pseudomonas, Bacillus, and Trichoderma genera. Subsequent microbiological studies by Wedemeyer (1968) revealed that Aerobacter aerogenes also will alter dieldrin similarly to 6,7- trans-dihydroxydihydroaldrin. Chacko, et al. (1966) tested this capability of 17 species of fungi and actinomycetes. Though most degraded pentachloronitrobenzene (PCNE) or DDT or both, none degraded dieldrin.

Patil, et al. (1972), studied the metabolic transformations of aldrin/dieldrin by marine algae, surface film, sediments, and water. They found that the insecticide was not degraded or metabolized in sea water or polluted waters. Some marine algal populations were shown to degrade aldrin to dieldrin.

Alterations of dieldrin by bacterial systems result in the formation of at least one acidic product (Matsumura and Boush, 1967). Once in the fatty tissue of organisms, dieldrin remains stable, according to Sanborn and Yu (1973). However, dieldrin can be mobilized from fatty tissue as demonstrated by Brockway (1973); for example, when fish are placed in an environment without dieldrin, there is an elimination from the tissue (Brockway, 1973). The elimination rate depends upon the diet with fasted fish eliminating dieldrin more rapidly than fed fish because of the utilization of fat stores (Grzenda, et al. 1972).

The dieldrin eliminated from the tissues reenters the water and thus becomes available for bioconcentration by other organisms. The movement of dieldrin among organisms, water, and sediment is dynamic, with equilibrium attained when the chemical concentration is constant.

REFERENCES

Brockway, D.C. 1973. The uptake, storage and release of dieldrin and some effects of its release in the fish, Cichlosoma bimaculatum (Linnaeus). Diss. Abstr. Int. 33: 4323B.

Chacko, C.I., et al. 1966. Chlorinated hydrocarbon pesticides: Degradation by microbes. Science. 154: 893.

Edwards, C.A. 1966. Insecticide residues in soils. Residue Rev. 13: 83.

Gakstatter, J.H. 1968. Rates of accumulation of 14C-dieldrin residues in tissues of goldfish exposed to a single sublethal dose of 14C-aldrin. Jour. Fish. Res. Board Can. 25: 1797.

Grzenda, A.R., et al. 1972. The elimination and turnover of 14C-dieldrin by different goldfish tissues. Trans. Am. Fish. Soc. 101: 686.

International Agency for Research on Cancer. 1974. Dieldrin. IARC monographs on the evaluation of carcinogenic risk of chemicals to man: Some organochlorine pesticides. 5: 125.

Matsumura, F., and G.M. Boush. 1967. Dieldrin: Degradation by soil microorganisms. Science. 156: 959.

Nash, R.G., and E.A. Woolson. 1967. Persistence of chlorinated hydrocarbon insecticides in soils. Science. 157: 924.

Patil, K.C., et al. 1972. Metabolic transformation of DDT, dieldrin, aldrin, and endrin by marine microorganisms. Environ. Sci. Technol. 6: 631.

Sanborn, J.R., and C.C. Yu. 1973. The fate of dieldrin in a model ecosystem. Bull. Environ. Contam. Toxicol. 10: 340.

Wedemyer, G. 1968. Partial hydrolysis of dieldrin by Aerobacter aerogenes. Appl. Microbiol. 16: 661.

Westlake, W.E., and J.P. San Antonio. 1960. Insecticide Residues in Plants, Animals and Soils. In: The Nature and Fate of Chemicals Applied to Soils, Plants, and Animals. U.S. Dep. Agric. 20: 9.

Aquatic Life Toxicology*

INTRODUCTION

Aldrin and dieldrin are members of a group of synthetic cyclic hydrocarbons called cyclodienes. The group includes other insecticides such as chlordane, heptachlor, endosulfan, and endrin. Until recently, aldrin and dieldrin were the most widely used domestic pesticides, with aldrin being applied in much greater quantities than dieldrin. Aldrin was applied to soils and foliage using soil injection or aerial techniques. Since leaching by water was minimal, soil erosion and sediment transport were the two major routes for aldrin to enter aquatic environments. However, these pesticides are often considered together because aldrin is rapidly converted to dieldrin by metabolism by animals and plants or by photodecomposition. This conversion is accomplished through the addition of an epoxide group to the aldrin molecule.

Since aldrin is rapidly converted to dieldrin and since adequate data are not available for the species required by the methodology, no criterion has been developed for aldrin. The following discussion is based on dieldrin data only except where specifically noted otherwise.

EFFECTS

Acute Toxicity

Results of 14 freshwater acute toxicity tests on dieldrin and invertebrate species are presented in Table 1. All of these tests were conducted under static conditions, and concentrations were not measured. The results ranged from a 96-hour LC_{50} value of 5.0 μg/l for the isopod Asellus brevicaudus to 740 μg/l for a crayfish (Sanders, 1972). This range of about 150 times demonstrates definite differences in species sensitivity to this compound.

---

*The reader is referred to the Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life and Its Uses in order to understand this section better. The attached tables contain pertinent available data, and at the bottoms of the appropriate tables are calculations deriving various measures of toxicity as described in the Guidelines.

Results of 12 acute toxicity tests with freshwater invertebrate species and aldrin are also presented in Table 1. Each test was conducted so that data could be compared with data obtained from comparable tests with dieldrin. Aldrin 96-hour LC_{50} values range from 8 μg/l for an isopod (Sanders, 1972) to 38,500 μg/l for the scud, Gammarus lacustris (Gaufin, et al. 1965). Generally, the LC_{50} values for aldrin are higher than those for dieldrin, except for cladoceran species which are more sensitive to aldrin.

Sixty-five acute toxicity tests on dieldrin and freshwater fish species are reported in Table 1. The tests were conducted with eight species of fishes including both coldwater and warmwater fishes. All of the tests were static, and none included measured concentrations.

The most sensitive fish species tested was the rainbow trout with 96-hour LC_{50} values between 1.1 and 9.9 μg/l. The other salmonids, coho and chinook salmon, had 96-hour LC_{50} values of 10.8 and 6.1 μg/l, respectively. The most resistant fish species was the goldfish with a 96-hour LC_{50} value of 41 μg/l. In the middle of the range, between the salmonids and the goldfish, were fathead minnows (range 16 to 36 μg/l) and the bluegill (range 8 to 32 μg/l). Special attention should be given to the data on the guppy in the report by Chadwick and Kiigemagi (1968) concerning the development of a toxicant delivery system. To determine the efficiency of the system, toxicity tests with the guppy were conducted over an extended time period, and the data are included in Table 1. Thirty-eight of the sixty-five test results are from this study; they range from 2.3 to 10 μg/l.

Twenty tests were conducted on aldrin with 12 freshwater fish species. The range of the 96-hour LC_{50} values (2.2 to 45.9 µg/l) is similar to the range (1.1 to 41 µg/l) obtained for dieldrin. Comparison of results from tests on both aldrin and dieldrin with the same fish species by the same author shows that the toxicities of these two chemicals to a given fish species are generally very similar (Henderson, et al. 1959; Katz, 1961; Macek, et al. 1969).

Acute toxicity tests with aldrin and dieldrin have established that these compounds are toxic to freshwater aquatic life at low concentrations. Based on species mean acute values summarized in Table 3, the Freshwater Final Acute Value for dieldrin, derived from the species mean acute values using the procedure described in the Guidelines, is 2.5 µg/l. Similarly, the Freshwater Final Acute Value for aldrin is 3.0 µg/l.

Saltwater invertebrate species are acutely sensitive to both aldrin and dieldrin, but there are greater differences in reported LC_{50} values for these species than for saltwater fish species (Table 1). Saltwater invertebrate acute values ranged from 0.37 to 33.0 µg/l for aldrin and from 0.28 to 50 µg/l for dieldrin (Tables 1 and 6). The most sensitive species to aldrin in a 96-hour test (Table 1) was Korean shrimp with LC_{50} values of 0.74 and 3.0 µg/l (Schoettger, 1970). The commercially important pink shrimp was the most sensitive species to dieldrin in a 96-hour test (Table 1) with an LC_{50} value of 0.7 µg/l (Parrish, et al. 1973). Other invertebrate species were less sensitive to dieldrin, and their acute LC_{50} values ranged from 3.7 to 50 µg/l (Table 1).

All species of saltwater fishes tested were sensitive to acute exposures to aldrin or dieldrin (Table 1). In aldrin exposures, the 96-hour LC_{50} values for 11 fish species ranged from 2.03 µg/l for dwarf perch (Earnest and Benville, 1972) to 100 µg/l for striped mullet (Eisler, 1970b). The acute LC_{50} values for 13 fish species exposed to dieldrin ranged from 0.9 µg/l for American eel to 34.0 µg/l for northern puffer (Eisler, 1970b). Generally, the LC_{50} values for aldrin are slightly higher than those for dieldrin in tests where the same species were tested.

Based on species mean acute values summarized in Table 3, the Saltwater Final Acute Value for dieldrin is 0.71 µg/l as calculated according to the procedure described in the Guidelines; that for aldrin is 1.3 µg/l.

Chronic Toxicity

Only one chronic study with a freshwater invertebrate species was found. Adema (1978) exposed the cladoceran, Daphnia magna, to dieldrin in a life-cycle test; a chronic value of 57 µg/l was obtained from his results. This value was not used in determining final chronic values because no acute toxicity information for D. magna was available in the literature, and the acute-chronic ratio required by the Guidelines could not be calculated.

Two chronic toxicity tests with freshwater fish species have been conducted with dieldrin. One was an early-life-stage exposure using steelhead (rainbow) trout (Chadwick and Shumway, 1969). A chronic value of 0.22 µg/l was calculated from their data. This was the most sensitive freshwater species according to the acute studies (Table 3). Because Chadwick and Shumway did not provide an acute value for this species, the species mean acute value of 2.5 µg/l is divided by the chronic value of 0.22 µg/l to give an acute-chronic ratio of 11 for this species (Table 2). The other chronic exposure was a three-generation study using the guppy (Roelofs, 1971). A chronic value of 0.45 µg/l was obtained. The geometric mean of 38 96-hour LC_{50} values (Table 1) using the same source of test water is 4.1 µg/l (Chadwick and Kiigemagi, 1969); the acute-chronic ratio is 9.1 (Table 2).

No chronic studies were found for any freshwater invertebrate species, other than *Daphnia magna* previously discussed. Based on measured concentrations however, Jensen and Gaufin (1966) determined a 30-day LC_{50} value of 2 µg/l for the stonefly, *Pteronarcys californica*, (Table 6) in flowing water, their typical habitat. This compares to an acute value of 39 µg/l (Jensen and Gaufin, 1966) from a static test in which concentrations were not measured. A lower 30-day LC_{50} value of 0.2 µg/l was also obtained for another stonefly, *Acroneuria pacifica* (Table 6). These data indicate that some chronic values for larval insects may be lower than those determined for fishes, which might be expected because the primary use of dieldrin was as an insecticide.

The only chronic data found for saltwater species was a 28-day life cycle study on the mysid shrimp with dieldrin (Table 2). In that study (U.S. EPA, 1980) the chronic limits were 0.49 and 1.1 µg/l based on cumulative mortality. Effects on reproduction (fecundity) were not observed in any of the test concentrations. The geometric mean of these two values, 0.73 µg/l, becomes the chronic value for mysid shrimp. Dividing this value into the acute value for this species of 4.5 µg/l gives an acute-chronic ratio of 6.2 (Table 2).

The Final Acute-Chronic Ratio for dieldrin of 8.5 is the geometric mean of the three acute-chronic ratios (Tables 2 and 3). The Freshwater Final Acute Value for dieldrin of 2.5 µg/l divided by the Final Acute-Chronic Ratio of 8.5 results in the Freshwater Final Chronic Value for dieldrin of 0.29 µg/l. The Saltwater Final Acute Value for dieldrin of 0.71 µg/l divided by the Final Acute-Chronic Ratio of 8.5 results in the Saltwater Final Chronic Value for dieldrin of 0.084 µg/l.

Plant Effects

Four toxicity tests have been conducted on dieldrin with three freshwater plant species (Table 4). The alga, Scenedesmus quadricaudata, was the most sensitive species tested with a 22 percent reduction in biomass after exposure to 100 µg/l (Stadnyk and Campbell, 1971). The other species, a diatom and the water-meal, were affected only at concentrations of 128 times and 100 times higher than that affecting the alga. Because fish and invertebrate species were affected at concentrations over 100 times lower than that affecting the alga, the plants should be protected by the animal-derived criteria.

Information on the sensitivity of saltwater aquatic plants, including algae and phytoplankton (Table 4), indicates, as was true for freshwater species, that they are much less sensitive than are saltwater fish and invertebrate species. Productivity and growth rates were reduced at concentrations of approximately 950 to 1,000 µg/l in three 4- to 36-hour static tests using one algal species and mixed population communities (Batterton, et al. 1971; Butler, 1963).

Residues

Table 5 contains the results of 11 freshwater residue studies with dieldrin. No comparable aldrin data were found. The 11 studies include plant, invertebrate, and fish species. The range of the bioconcentration factors (BCF) is from 128 for an alga (Reinert, 1972) to 68,286 for whole body of yearling lake trout (Reinert, et al. 1974). All of the authors (except Reinert, et al. 1974) indicate that a steady-state condition was reached in their studies.

The analysis of the freshwater residue data can be divided into two broad groups, the plant-invertebrate and the fish data. The lower plant-invertebrate BCF values range from 128 to 5,558. The two values representing the algal and diatom community accumulations are perhaps the most ecologically applicable data in this group. The studies were conducted in open channels under field conditions, whereas the other algal study was a short-exposure laboratory test. The two BCF values for invertebrate species show a comparatively low bioaccumulation potential.

The BCF values for freshwater fish species range from 2,385 to 68,286. Although all but one of the authors reported that steady-state had been reached in each of their exposures, there seems to be a relationship between length of exposure and total residue accumulation. For example, guppies exposed for 32 days had a BCF of 12,708, whereas exposure for 160 to 230 days resulted in a BCF of 28,408. The same relationship may explain the high BCF for the lake trout. The bioconcentration of dieldrin by this species may become greater since the fish may not have reached steady-state when the study was terminated. The channel catfish BCF is the lowest of the values for fish species (Shannon, 1977a,b). This is probably a result of the experimenter analyzing dorsal muscle rather than whole fish (with its higher lipid content) as was done by the others.

Bioconcentration factors for dieldrin and saltwater species (Tables 5 and 6) range from 400 to 8,000 for fish or shellfish (Lane and Livingston, 1970; Epifanio, 1973; Parrish, et al. 1973; Parrish, 1974; Mason and Rowe, 1976). Bioconcentration factors for oysters were higher for longer exposure periods because dieldrin concentrations in tissues reached steady-state conditions after extended periods (several weeks) of exposure (Parrish, 1974; Mason and Rowe, 1976). Therefore, long exposures are necessary to attain steady-state bioconcentration factors. After 34 weeks of exposure to dieldrin, sailfin mollies exhibited BCF values of 2,867 to 4,867 in muscle; values for liver, brain, gill, intestine, and blood ranged from 10,500 to 50,000 (Lane and Livingston, 1970). Spot exposed to dieldrin for 35 days depurated the chemical to non-detectable body-burdens within 13 days of holding in dieldrin-free saltwater (Parrish, et al. 1973). Concentrations in edible tissues were about 15 percent less than concentrations in whole spot; however, concentrations in liver were 2 to 13 times that in spot muscle.

Dividing a BCF value by the percent lipid value for the same species provides a BCF value based on one percent lipid content: this resultant BCF value is referred to as the normalized BCF. The two BCF values for which percent lipid data are available (1,160 for freshwater mussel and 2,300 for spot) (Table 5) were normalized by dividing the BCF values by their corresponding percent lipid values. The geometric mean of the normalized BCF values was then calculated to be 1,557. The action level established by the U.S. Food and Drug Administration (FDA) for dieldrin in fish and shellfish is 0.3 mg/kg. Dividing the FDA action level of 0.3 mg/kg by the geometric mean of normalized BCF values (1,557) and by a percent lipid value of 15 for freshwater species (see Guidelines) gives a freshwater residue value of 0.013 µg/l. Similarly, dividing the FDA action level of 0.3 mg/kg by the geometric mean of normalized BCF values (1,557) and by a percent lipid value of 16 for saltwater species (see Guidelines) gives a saltwater residue value of 0.012 µg/l. The highest BCF value for the edible portion of a consumed freshwater species is 2,993 for channel catfish (Shannon, 1977a). Dividing this value into the FDA action level of 0.3 mg/kg gives a freshwater residue value of 0.10 µg/l. The highest BCF value for the edible portion of a consumed saltwater species is the value of 8,000 for Eastern oyster (Parrish, 1974). Dividing this into the FDA action level of 0.3 mg/kg gives a saltwater residue value of 0.038 µg/l.

The U.S. FDA has established an action level of 0.3 mg/kg for dieldrin in fish oil. Dividing this value by the geometric mean of normalized BCF values (1,557) and by a percent lipid value of 100 for fish oil gives a residue value of 0.0019 µg/l for both freshwater and saltwater.

The lowest residue value of those calculated is 0.0019 µg/l, and this value is then the Freshwater Final Residue Value and Saltwater Final Residue Value (Table 5) The Final Residue Value may be too high because, on the average, the concentration in 50 percent of species similar to those used to derive the value will exceed the FDA action level.

Miscellaneous

The freshwater data presented in Table 6 do not conflict with data used to calculate the Freshwater Final Acute and Chronic Value. However, a special sensitivity of aquatic insects to dieldrin is reflected in the values obtained in 30-day exposures of *Pteronarcys dorsata* and *Acroneuria pacifica*. With these insects the LC_{50} values were 2 and 0.2 µg/l, respectively. A 24-hour exposure of the midge, *Chironomus tentans*, resulted in an LC_{50} of 0.9 µg/l. These three values are below the Final Acute Value of 2.5 µg/l, which indicates that some aquatic insects may not be protected by this value.

For saltwater species, two pink shrimp studies by Lowe (undated)(Table 6) give acute values for aldrin (0.37 µg/l) and dieldrin (0.28 µg/l) that are lower than any in Table 1. Parrish, et al. (1973) produced an LC_{50} value of 0.7 µg/l dieldrin for pink shrimp based on measured values in a flow-through test; this test should take precedence over that of Lowe, in which the test concentrations were not measured. If one can assume that the relationship between the dieldrin LC_{50} values for Korean shrimp (flow-through test) and pink shrimp (i.e., 6.9 to 0.7 µg/l) would hold for the same two species exposed to aldrin, then one would expect the aldrin LC_{50} for pink shrimp to be 1/10 that (3.0 µg/l) of Korean shrimp, or 0.3 µg/l. In fact, a 24-hour EC_{50} of 0.37 µg/l has been reported for pink shrimp (Lowe, undated)(Table 6). Because this test does not meet the criteria in the Guidelines for an acceptable acute test (the duration was 24 hours), it was not placed in Table 1. However, pink shrimp are commercially valuable as well as ecologically important, and the Saltwater Final Acute Value may be too high to protect this important species.

Summary

Acute values are available for 19 freshwater fish and invertebrate species. The data are all from static exposures in which aldrin and dieldrin concentrations were calculated but not measured. The species list represents all of the major functional and taxonomic classifications. The most resistant fish species is the goldfish at 41 µg/l, and the most sensitive is the rainbow trout at 2.5 µg/l. A similar comparison for the invertebrate species shows a range from 5 µg/l for the isopod, Asellus brevicaudus, to 39 µg/l for the stonefly, Pteronarcys californica. The Freshwater Final Acute Value for dieldrin is 2.5 µg/l; that for aldrin is 3.0 µg/l.

The three freshwater chronic values for dieldrin are 0.22, 0.45, and 57 µg/l for the rainbow trout, guppy, and Daphnia magna, respectively. The acute-chronic ratios for rainbow trout and guppy are 11 and 9.1, respectively.

The freshwater residue data for dieldrin show a wide range of bioconcentration factors. The highest factor was for yearling lake trout which may not have reached steady-state at a bioconcentration factor of 68,286. This factor may underestimate the bioconcentration potential of older, larger lake trout and thus is a conservative estimate for this species. The Freshwater Final Residue Value for dieldrin of 0.0019 µg/l was calculated using the FDA action level of 0.3 mg/kg for fish oil, a percent lipid value of 100 for fish oil, and the geometric mean of normalized bioconcentration factors (1,557). The Final Residue Value may be too high because, on the average, the concentration in 50 percent of species similar to those used to derive the value will exceed the FDA action.

The freshwater plant data clearly indicate that plants are more resistant than animals. The lowest plant value of 100 µg/l for 10 days would certainly destroy most animal life in the water.

The acute toxicities of aldrin and dieldrin to saltwater organisms and the persistence and bioaccumulation potential for dieldrin have been studied using saltwater plants and animals. Bioaccumulation by saltwater organisms and/or subsequent transfer to other animals in saltwater food-webs have been documented in field studies and laboratory experiments. Results from >96-hour tests indicate that dieldrin is chronically toxic to saltwater fishes and crabs, although the exact mechanism of toxicity is not known. The Saltwater Final Acute Value for dieldrin is 0.71 µg/l; that for aldrin is 1.3 µg/l.

No chronic study on any saltwater fish species has been reported. One saltwater test on dieldrin using the mysid shrimp, Mysidopsis bahia, produced a chronic value of 0.73 µg/l, and the acute-chronic ratio for the species is 6.2. The Saltwater Final Chronic Value for dieldrin is 0.084 µg/l.

Dieldrin bioconcentration factors for saltwater species range from 400 to 8,000. The Saltwater Final Residue Value of 0.0019 µg/l was calculated using the FDA action level of 0.3 mg/kg for fish oil, a percent lipid value of 100 for fish oil, and the geometric mean of normalized bioconcentration factors (1,557). The Final Residue Value may be too high because, on the average, the concentration in 50 percent of species similar to those used to derive the criteria will exceed the FDA action level.

CRITERIA

Dieldrin

For dieldrin, the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.0019 µg/l as a 24-hour average, and the concentration should not exceed 2.5 µg/l at any time.

For dieldrin the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.0019 µg/l as a 24-hour average, and the concentration should not exceed 0.71 µg/l at any time.

Aldrin

For freshwater aquatic life, the concentration of aldrin should not exceed 3.0 µg/l at any time. No data are available concerning the chronic toxicity of aldrin to sensitive freshwater aquatic life.

For saltwater aquatic life, the concentration of aldrin should not exceed 1.3 µg/l at any time. No data are available concerning the chronic toxicity of aldrin to sensitive saltwater aquatic life.

Table 1. Acute values for aldrin/dieldrin

Species	Method*	Chemical	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
FRESHWATER SPECIES					
Cladoceran, Daphnia carinata	S, U	Technical grade dieldrin	130	130	Santharam, et al. 1976
Cladoceran, Daphnia pulex	S, U	Dieldrin	250	250	Sanders & Cope, 1966
Cladoceran, Simocephalus serrulatus	S, U	Dieldrin	240	-	Sanders & Cope, 1966
Cladoceran, Simocephalus serrulatus	S, U	Dieldrin	190	213	Sanders & Cope, 1966
Isopod, Asellus brevicaudus	S, U	Dieldrin	5	5	Sanders, 1972
Scud, Gammarus fasciatus	S, U	Dieldrin	640	-	Sanders, 1972
Scud, Gammarus fasciatus	S, U	Dieldrin	600	620	Sanders, 1972
Scud, Gammarus lacustris	S, U	Dieldrin	700	-	Gaufin, et al. 1965
Scud, Gammarus lacustris	S, U	Dieldrin	460	567	Sanders, 1969
Glass shrimp, Palaemonetes kadiakensis	S, U	Dieldrin	20	20	Sanders, 1972
Crayfish, Orconectes nais	S, U	Dieldrin	740	740	Sanders, 1972
Mayfly, Ephemerella grandis	S, U	Dieldrin	8	8	Gaufin, et al. 1965
Stonefly, Acroneuria pacifica	S, U	100% dieldrin	24	24	Jensen & Gaufin, 1964

Table 1. (Continued)

Species	Method*	Chemical	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Stonefly, *Pteronarcys californica*	S, U	100% dieldrin	39	39	Jensen & Gaufin, 1964
Rainbow trout, *Salmo gairdneri*	S, U	90% dieldrin	9.9	-	Katz, 1961
Rainbow trout, *Salmo gairdneri*	S, U	85% dieldrin	2.4	-	Macek, et al. 1969
Rainbow trout, *Salmo gairdneri*	S, U	85% dieldrin	1.1	-	Macek, et al. 1969
Rainbow trout, *Salmo gairdneri*	S, U	85% dieldrin	1.4	2.5	Macek, et al. 1969
Coho salmon, *Oncorhynchus kisutch*	S, U	90% dieldrin	10.8	10.8	Katz, 1961
Chinook salmon, *Oncorhynchus tshawytscha*	S, U	90% dieldrin	6.1	6.1	Katz, 1961
Goldfish, *Carassius auratus*	S, U	90% dieldrin	41	41	Henderson, et al. 1959
Fathead minnow, *Pimephales promelas*	S, U	90% dieldrin	18	-	Henderson, et al. 1959
Fathead minnow, *Pimephales promelas*	S, U	90% dieldrin	18	-	Henderson, et al. 1959
Fathead minnow, *Pimephales promelas*	S, U	85% dieldrin	36	-	Tarzwell & Henderson, 1957
Fathead minnow, *Pimephales promelas*	S, U	85% dieldrin	24	-	Tarzwell & Henderson, 1957
Fathead minnow, *Pimephales promelas*	S, U	85% dieldrin	16	-	Tarzwell & Henderson, 1957
Fathead minnow, *Pimephales promelas*	S, U	85% dieldrin	25	-	Tarzwell & Henderson, 1957

Table 1. (Continued)

Species	Method*	Chemical	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Fathead minnow, *Pimephales promelas*	S, U	85% dieldrin	23	22	Tarzwell & Henderson, 1957
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	3.9	-	Chadwick & Kilgemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	4.7	-	Chadwick & Kilgemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	3.9	-	Chadwick & Kilgemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	5.1	-	Chadwick & Kilgemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	3.9	-	Chadwick & Kilgemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	3.7	-	Chadwick & Kilgemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	3.2	-	Chadwick & Kilgemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	3.9	-	Chadwick & Kilgemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	4.2	-	Chadwick & Kilgemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	4.3	-	Chadwick & Kilgemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	4.3	-	Chadwick & Kilgemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	4.1	-	Chadwick & Kilgemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	3.5	-	Chadwick & Kilgemagi, 1968

Table 1. (Continued)

Species	Method*	Chemical	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	4.7	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	3.2	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	2.9	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	2.6	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	2.9	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	2.4	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	2.6	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	2.3	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	2.7	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	2.3	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	2.7	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	2.7	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	4.8	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	6.1	-	Chadwick & Kiigemagi, 1968

Table 1. (Continued)

Species	Method*	Chemical	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Guppy, *Poecilia reticulata*	S, U	Technical grade dieldrin	3.2	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	99+% dieldrin	6.6	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	99+% dieldrin	5.6	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	99+% dieldrin	6.1	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	99+% dieldrin	7.5	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	99+% dieldrin	10	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	99+% dieldrin	6.6	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	99+% dieldrin	6.6	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	99+% dieldrin	6.9	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	99+% dieldrin	4.7	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	99+% dieldrin	7.5	-	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S, U	90% dieldrin	25	-	Henderson, et al. 1959
Guppy, *Poecilia reticulata*	S, U	Dieldrin	21	4.5	Cairns & Loos, 1966
Green sunfish, *Lepomis cyanellus*	S, U	85% dieldrin	6	-	Tarzwell & Henderson, 1957

Table 1. (Continued)

Species	Method*	Chemical	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Green sunfish, *Lepomis cyanellus*	S, U	85% dieldrin	11	-	Tarzwell & Henderson, 1957
Green sunfish, *Lepomis cyanellus*	S, U	85% dieldrin	8	8.1	Tarzwell & Henderson, 1957
Bluegill, *Lepomis macrochirus*	S, U	90% dieldrin	9	-	Henderson, et al. 1959
Bluegill, *Lepomis macrochirus*	S, U	85% dieldrin	17	-	Macek, et al. 1969
Bluegill, *Lepomis macrochirus*	S, U	85% dieldrin	14	-	Macek, et al. 1969
Bluegill, *Lepomis macrochirus*	S, U	85% dieldrin	8.8	-	Macek, et al. 1969
Bluegill, *Lepomis macrochirus*	S, U	85% dieldrin	32	-	Tarzwell & Henderson, 1957
Bluegill, *Lepomis macrochirus*	S, U	85% dieldrin	18	-	Tarzwell & Henderson, 1957
Bluegill, *Lepomis macrochirus*	S, U	85% dieldrin	8	-	Tarzwell & Henderson, 1957
Bluegill, *Lepomis macrochirus*	S, U	85% dieldrin	22	15	Tarzwell & Henderson, 1957
Cladoceran, *Daphnia pulex*	S, U	Aldrin	28	28	Sanders & Cope, 1966
Cladoceran, *Simocephalus serrulatus*	S, U	Aldrin	23	-	Sanders & Cope, 1966
Cladoceran, *Simocephalus serrulatus*	S, U	Aldrin	32	27	Sanders & Cope, 1966
Isopod, *Asellus brevicaudus*	S, U	Aldrin	8	8	Sanders, 1972

Table 1. (Continued)

Species	Method*	Chemical	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Scud, *Gammarus fasciatus*	S, U	Aldrin	4,300	-	Sanders, 1972
Scud, *Gammarus fasciatus*	S, U	Aldrin	5,600	4,900	Sanders, 1972
Scud, *Gammarus lacustris*	S, U	Aldrin	38,500	-	Gaufin, et al. 1965
Scud, *Gammarus lacustris*	S, U	Aldrin	9,800	19,000	Sanders, 1969
Glass shrimp, *Palaemonetes kadiakensis*	S, U	Aldrin	50	50	Sanders, 1972
Mayfly, *Ephemerella grandis*	S, U	Aldrin	9	9	Gaufin, et al. 1965
Stonefly, *Acroneuria pacifica*	S, U	Aldrin	143	143	Jensen & Gaufin, 1964
Stonefly, *Pteronarcys californica*	S, U	93% aldrin	180	180	Jensen & Gaufin, 1964
American eel, *Anguilla rostrata*	S, U	Aldrin	16	16	Rehwoldt, et al. 1977
Rainbow trout, *Salmo gairdneri*	S, U	88.4% aldrin	17.7	-	Katz, 1961
Rainbow trout, *Salmo gairdneri*	S, U	95% aldrin	3.2	-	Macek, et al. 1969
Rainbow trout, *Salmo gairdneri*	S, U	95% aldrin	3.3	-	Macek, et al. 1969
Rainbow trout, *Salmo gairdneri*	S, U	95% aldrin	2.2	4.5	Macek, et al. 1969
Coho salmon, *Oncorhynchus kisutch*	S, U	88.4% aldrin	45.9	45.9	Katz, 1961

Table 1. (Continued)

Species	Method*	Chemical	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Chinook salmon, *Oncorhynchus tshawytscha*	S, U	88.4% aldrin	6.1	6.1	Katz, 1961
Goldfish, *Carassius auratus*	S, U	88.4% aldrin	32	32	Henderson, et al. 1959
Carp, *Cyprinus carpio*	S, U	Aldrin	4	4	Rehwoldt, et al. 1977
Fathead minnow, *Pimephales promelas*	S, U	88.4% aldrin	37	-	Henderson, et al. 1959
Fathead minnow, *Pimephales promelas*	S, U	88.4% aldrin	32	34	Henderson, et al. 1959
Banded killifish, *Fundulus diaphanus*	S, U	Aldrin	21	21	Rehwoldt, et al. 1977
Guppy, *Poecilia reticulata*	S, U	88.4% aldrin	37	-	Henderson, et al. 1959
Guppy, *Poecilia reticulata*	S, U	Aldrin	20	27	Rehwoldt, et al. 1977
White perch, *Roccus americanus*	S, U	Aldrin	42	42	Rehwoldt, et al. 1977
Striped bass, *Morone saxatilis*	S, U	Aldrin	10	10	Rehwoldt, et al. 1977
Bluegill, *Lepomis macrochirus*	S, U	88.4% aldrin	15	-	Henderson, et al. 1959
Bluegill, *Lepomis macrochirus*	S, U	95% aldrin	7.7	-	Macek, et al. 1969
Bluegill, *Lepomis macrochirus*	S, U	95% aldrin	5.8	-	Macek, et al. 1969
Bluegill, *Lepomis macrochirus*	S, U	95% aldrin	4.6	7.4	Macek, et al. 1969

Table 1. (Continued)

Species	Method*	Chemical	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
		SALTWATER SPECIES			
Eastern oyster, *Crassostrea virginica*	FT, U	Dieldrin	34**	-	Butler, 1963
Eastern oyster, *Crassostrea virginica*	FT, M	Dieldrin	31.2**	31.2	Parrish, et al. 1973
Mysid shrimp, *Mysidopsis bahia*	S, U	Dieldrin	3.7	-	U.S. EPA, 1980
Mysid shrimp, *Mysidopsis bahia*	FT, M	Dieldrin	4.5	4.5	U.S. EPA, 1980
Sand shrimp, *Crangon septemspinosa*	S, U	Dieldrin	7.0	7.0	Eisler, 1969
Hermit crab, *Pagurus longicarpus*	S, U	Dieldrin	18.0	18.0	Eisler, 1969
Grass shrimp, *Palaemonetes vulgaris*	S, U	Dieldrin	50.0	50.0	Eisler, 1969
Grass shrimp, *Palaemonetes pugio*	FT, M	Dieldrin	8.6	8.6	Parrish, et al. 1973
Korean shrimp, *Palaemon macrodactylus*	S, U	Dieldrin	16.9	-	Schoettger, 1970
Korean shrimp, *Palaemon macrodactylus*	FT, U	Dieldrin	6.9	10.8	Schoettger, 1970
Pink shrimp, *Penaeus duorarum*	FT, M	Dieldrin	0.7	0.7	Parrish, et al. 1973
American eel, *Anguilla rostrata*	S, U	Dieldrin	0.9	0.9	Eisler, 1970b
Chinook salmon, *Oncorhynchus tshawytscha*	FT, U	Dieldrin	1.5	1.5	Schoettger, 1970
Atlantic silverside, *Menidia menidia*	S, U	Dieldrin	5.0	5.0	Eisler, 1970b

Table 1. (Continued)

Species	Method*	Chemical	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Sheepshead minnow, *Cyprinodon variegatus*	FT, M	Dieldrin	10.0	10.0	Parrish, et al. 1973
Mummichog, *Fundulus heteroclitus*	S, U	Dieldrin	5.0	-	Eisler, 1970a
Mummichog, *Fundulus heteroclitus*	S, U	Dieldrin	16.0	8.9	Eisler, 1970b
Striped killifish, *Fundulus majalis*	S, U	Dieldrin	5.0	5.0	Eisler, 1970b
Threespine stickleback, *Gasterosteus aculeatus*	S, U	Dieldrin	15.3	-	Katz, 1961
Threespine stickleback, *Gasterosteus aculeatus*	S, U	Dieldrin	13.1	14.2	Katz, 1961
Striped bass, *Morone saxatilis*	FT, U	Dieldrin	19.7	19.7	Korn & Earnest, 1974
Shiner perch, *Cymatogaster aggregata*	S, U	Dieldrin	3.7	-	Earnest & Benville, 1972
Shiner perch, *Cymatogaster aggregata*	FT, U	Dieldrin	1.5	2.3	Earnest & Benville, 1972
Dwarf perch, *Micrometrus minimus*	S, U	Dieldrin	5.0	-	Earnest & Benville, 1972
Dwarf perch, *Micrometrus minimus*	FT, U	Dieldrin	2.44	3.5	Earnest & Benville, 1972
Bluehead, *Thalassoma bifasciatum*	S, U	Dieldrin	6.0	6.0	Eisler, 1970b
Striped mullet, *Mugil cephalus*	S, U	Dieldrin	23.0	23.0	Eisler, 1970b
Northern puffer, *Sphaeroides maculatus*	S, U	Dieldrin	34.0	34.0	Eisler, 1970b

Table 1. (Continued)

Species	Method*	Chemical	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Eastern oyster, *Crassostrea virginica*	FT, U	Aldrin	25.0**	25.0	Butler, 1963
Sand shrimp, *Crangdon septemspinosa*	S, U	Aldrin	8.0	8.0	Eisler, 1969
Hermit crab, *Pagurus longicarpus*	S, U	Aldrin	33.0	33.0	Eisler, 1969
Grass shrimp, *Palaemonetes vulgaris*	S, U	Aldrin	9.0	9.0	Eisler, 1969
Korean shrimp, *Palaemon macrodactylus*	S, U	Aldrin	0.74	-	Schoettger, 1970
Korean shrimp, *Palaemon macrodactylus*	FT, U	Aldrin	3.0	1.5	Schoettger, 1970
American eel, *Anguilla rostrata*	S, U	Aldrin	5.0	5.0	Eisler, 1970b
Mummichog, *Fundulus heteroclitus*	S, U	Aldrin	8.0	-	Eisler, 1970b
Mummichog, *Fundulus heteroclitus*	S, U	Aldrin	4.0	5.6	Eisler, 1970a
Striped killifish, *Fundulus majalis*	S, U	Aldrin	17.0	17.0	Eisler, 1970b
Atlantic silverside, *Menidia menidia*	S, U	Aldrin	13.0	13.0	Eisler, 1970b
Threespine stickleback, *Gasterosteus aculeatus*	S, U	Aldrin	39.8	-	Katz, 1961
Threespine stickleback, *Gasterosteus aculeatus*	S, U	Aldrin	27.4	33.0	Katz, 1961
Striped bass, *Morone saxatilis*	FT, U	Aldrin	7.2	7.2	Korn & Earnest, 1974

Table 1. (Continued)

Species	Method*	Chemical	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Shiner perch, *Cymatogaster aggregata*	S, U	Aldrin	7.4	-	Earnest & Benville, 1972
Shiner perch, *Cymatogaster aggregata*	FT, U	Aldrin	2.26	4.1	Earnest & Benville, 1972
Dwarf perch, *Micrometrus minimus*	S, U	Aldrin	18.0	-	Earnest & Benville, 1972
Dwarf perch, *Micrometrus minimus*	FT, U	Aldrin	2.03	6.0	Earnest & Benville, 1972
Bluehead, *Thalassoma bifasciatum*	S, U	Aldrin	12.0	12.0	Eisler, 1970b
Striped mullet, *Mugil cephalus*	S, U	Aldrin	100.0	100.0	Eisler, 1970b
Northern puffer, *Sphaeroides maculatus*	S, U	Aldrin	36.0	36.0	Eisler, 1970b

---

* S = static, FT = flow-through, U = unmeasured, M = measured

**EC50 based on shell deposition

Table 2. Chronic values for dieldrin

Species	Test*	Limits (µg/l)	Chronic Value (µg/l)	Reference
		FRESHWATER SPECIES		
Cladoceran, *Daphnia magna*	LC	32-100	57	Adema, 1978
Rainbow trout, *Salmo gairdneri*	ELS	0.12-0.39	0.22	Chadwick & Shumway, 1969
Guppy, *Poecilia reticulata*	LC	0.2-1.0	0.45	Roelofs, 1971
		SALTWATER SPECIES		
Mysid shrimp, *Mysidopsis bahia*	LC	0.49-1.1	0.73	U.S. EPA, 1980

---

* LC = life cycle or partial life cycle, ELS = early life stage

Acute-Chronic Ratios

Species	Acute Value (µg/l)	Chronic Value (µg/l)	Ratio
Rainbow trout, *Salmo gairdneri*	2.5	0.22	11
Guppy, *Poecilia reticulata*	4.1	0.45	9.1
Mysid shrimp, *Mysidopsis bahia*	4.5	0.73	6.2

Table 3. Species mean acute values and acute-chronic ratios for aldrin/dieldrin

Rank*	Species	Species Mean Acute Value (µg/l)	Species Mean Acute-Chronic Ratio
		FRESHWATER SPECIES	
		Dieldrin	
19	Crayfish, *Orconectes nais*	740	-
18	Scud, *Gammarus fasciatus*	620	-
17	Scud, *Gammarus lacustris*	567	-
16	Cladoceran, *Daphnia pulex*	250	-
15	Cladoceran, *Simocephalus serrulatus*	213	-
14	Cladoceran, *Daphnia carinata*	130	-
13	Goldfish, *Carassius auratus*	41	-
12	Stonefly, *Pteronarcys californica*	39	-
11	Stonefly, *Acroneuria pacifica*	24	-
10	Fathead minnow, *Pimephales promelas*	22	-
9	Glass shrimp, *Palaemonetes kadiakensis*	20	-
8	Bluegill, *Lepomis macrochirus*	15	-
7	Coho salmon, *Oncorhynchus kisutch*	10.8	-

Table 3. (Continued)

Rank*	Species	Species Mean Acute Value (µg/l)	Species Mean Acute-Chronic Ratio
6	Green sunfish, *Lepomis cyanellus*	8.1	-
5	Mayfly, *Ephemerella grandis*	8	-
4	Chinook salmon, *Oncorhynchus tshawytscha*	6.1	-
3	Isopod, *Asellus brevicaudus*	5.0	-
2	Guppy, *Poecilia reticulata*	4.5	9.1
1	Rainbow trout, *Salmo gairdneri*	2.5	11
		Aldrin	
21	Scud, *Gammarus lacustris*	19,000	-
20	Scud, *Gammarus fasciatus*	4,900	-
19	Stonefly, *Pteronarcys californica*	180	-
18	Stonefly, *Acroneuria pacifica*	143	-
17	Glass shrimp, *Palaemonetes kadiakensis*	50	-
16	Coho salmon, *Oncorhynchus kisutch*	45.9	-
15	White perch, *Roccus americanus*	42	-

Table 3. (Continued)

Rank*	Species	Species Mean Acute Value (µg/l)	Species Mean Acute-Chronic Ratio
14	Fathead minnow, *Pimephales promelas*	34	-
13	Goldfish, *Carassius auratus*	32	-
12	Cladoceran, *Daphnia pulex*	28	-
11	Guppy, *Poecilia reticulata*	27	-
10	Cladoceran, *Simocephalus serrulatus*	27	-
9	Banded killifish, *Fundulus diaphanus*	21	-
8	American eel, *Anguilla rostrata*	16	-
7	Striped bass, *Morone saxatilis*	10	-
6	Mayfly, *Ephemerella grandis*	9	-
5	Isopod, *Asellus brevicaudus*	8	-
4	Bluegill, *Lepomis macrochirus*	7.4	-
3	Chinook salmon, *Oncorhynchus tshawytscha*	6.1	-
2	Rainbow trout, *Salmo gairdneri*	4.5	-
1	Carp, *Cyprinus carpio*	4	-

Table 3. (Continued)

Rank*	Species	Species Mean Acute Value (µg/l)	Species Mean Acute-Chronic Ratio
	SALTWATER SPECIES		
	Dieldrin		
21	Grass shrimp, *Palaemonetes vulgaris*	50.0	-
20	Northern puffer, *Sphaeroides maculatus*	34.0	-
19	Eastern oyster, *Crassostrea virginica*	31.2	-
18	Striped mullet, *Mugil cephalus*	23.0	-
17	Striped bass, *Morone saxatilis*	19.7	-
16	Hermit crab, *Pagurus longicarpus*	18.0	-
15	Threespine stickleback, *Gasterosteus aculatus*	14.2	-
14	Korean shrimp, *Palaemon macrodactylus*	10.8	-
13	Sheepshead minnow, *Cyprinodon variegatus*	10.0	-
12	Mummichog, *Fundulus heteroclitus*	8.9	-
11	Grass shrimp, *Palaemonetes pugio*	8.6	-
10	Sand shrimp, *Crangon septemspinosa*	7.0	-
9	Bluehead, *Thalassoma bifasciatum*	6.0	-

Table 3. (Continued)

Rank*	Species	Species Mean Acute Value (µg/l)	Species Mean Acute-Chronic Ratio
8	Striped killifish, *Fundulus majalis*	5.0	-
7	Atlantic silverside, *Menidia menidia*	5.0	-
6	Mysid shrimp, *Mysidopsis bahia*	4.5	6.2
5	Dwarf perch, *Micrometrus minimus*	3.5	-
4	Shiner perch, *Cyamatogaster aggregata*	2.3	-
3	Chinook salmon, *Oncorhynchus tshawytscha*	1.5	-
2	American eel, *Anguilla rostrata*	0.9	-
1	Pink shrimp, *Penaeus duorarum*	0.7	-
	Aldrin		
16	Striped mullet, *Mugil cephalus*	100.0	-
15	Northern puffer, *Sphaeroides maculatus*	36.0	-
14	Hermit crab, *Pagurus longicarpus*	33.0	-
13	Three-spined stickleback, *Gasterosteus aculeatus*	33.0	-
12	Eastern oyster, *Crassostrea virginica*	25.0	-

Table 3. (Continued)

Rank*	Species	Species Mean Acute Value (µg/l)	Species Mean Acute-Chronic Ratio
11	Striped killifish, *Fundulus majalis*	17.0	-
10	Atlantic silverside, *Menidia menidia*	13.0	-
9	Bluehead, *Thalassoma bifasciatum*	12.0	-
8	Grass shrimp, *Palaemonetes pulgaris*	9.0	-
7	Sand shrimp, *Crangon septemspinosa*	8.0	-
6	Striped bass, *Morone saxatilis*	7.2	-
5	Dwarf perch, *Micrometrus minimus*	6.0	-
4	Mummichog, *Fundulus heteroclitus*	5.6	-
3	American eel, *Anguilla rostrata*	5.0	-
2	Shiner perch, *Cymatogaster aggregata*	4.1	-
1	Korean shrimp, *Palaemon macrodactylus*	1.5	-

---

* Ranked from least sensitive to most sensitive based on species mean acute value.

Freshwater Final Acute Value for aldrin = 3.0 µg/l

Saltwater Final Acute Value for aldrin = 1.3 µg/l

Table 3. (Continued)

Final Acute-Chronic Ratio for dieldrin = 8.5

Freshwater Final Acute Value for dieldrin = 2.5 µg/l

Freshwater Final Chronic Value for dieldrin = 2.5 µg/l ÷ 8.5 = 0.29 µg/l

Saltwater Final Acute Value for dieldrin = 0.71 µg/l

Saltwater Final Chronic Value for dieldrin = 0.71 µg/l ÷ 8.5 = 0.084 µg/l

Table 4. Plant values for aldrin/dieldrin

Species	Chemical	Effect	Result (µg/l)	Reference
		FRESHWATER SPECIES		
Alga, *Scenedesmus quadricaudata*	Dieldrin	22% reduction in biomass in 10 days	100	Stadnyk & Campbell, 1971
Diatom, *Navicula seminulum*	Dieldrin	50% reduction in growth in 5 days	12,800	Cairns, 1968
Water-meal, *Wolffia papulifera*	Dieldrin	Reduced population growth in 12 days	10,000	Worthley & Schott, 1971
Water-meal, *Wolffia papulifera*	Aldrin	Reduced population growth in 12 days	10,000	Worthley & Schott, 1971
		SALTWATER SPECIES		
Alga, *Agmenellum quadruplicatum*	Dieldrin	Reduced growth ratio	950	Batterton, et al. 1971
Phytoplankton community	Aldrin	84.6-84.8% decrease in productivity after 4 hrs	1,000	Butler, 1963

Table 5. Residues for dieldrin

Species	Tissue	Lipid (%)	Bioconcentration Factor	Duration (days)	Reference
			FRESHWATER SPECIES		
Alga, Scenedesmus obliquus	-	-	128	2.5	Reinert, 1972
Community dominated by the alga, Tribonema minus	-	-	5,558	4-6 wks	Rose & McIntire, 1970
Community of alga and diatoms including Stigeoclonium subsecundum, Synedria ulna, Epithemia sorex, Cocconeis placentula var. euglypta, and Nitzschia sp.	-	-	3,188	4-6 wks	Rose & McIntire, 1970
Cladoceran, Daphnia magna	-	-	1,395	3	Reinert, 1972
Freshwater mussel, Lampsilis siliquoidea	whole body	1	1,160	7-12	Bedford & Zabik, 1973
Steelhead trout (newly hatched alevin), Salmo gairdneri	whole animal	-	3,225	35	Chadwick & Shumway, 1969
Lake trout (yearling), Salvelinus namaycush	whole body	-	68,286	152	Reinert, et al. 1974
Channel catfish, Ictalurus punctatus	dorsal muscle	-	2,385	70	Shannon, 1977b
Channel catfish, Ictalurus punctatus	dorsal muscle	-	2,993	28	Shannon, 1977a
Guppy, Poecilia reticulata	whole animal	-	12,708	32	Reinert, 1972
Guppy, Poecilia reticulata	whole animal	-	28,408	160-230	Roelofs, 1971

Table 5. (Continued)

Species	Tissue	Lipid (%)	Bioconcentration Factor	Duration (days)	Reference
			SALTWATER SPECIES		
Eastern oyster, Crassostrea virginica	edible tissue	-	8,000	392	Parrish, 1974
Crab, Leptodius floridanus	whole body	-	400*	16	Epifanio, 1973
Sailfin molly, Poecilia latipinna	edible tissue	-	4,867	238	Lane & Livingston, 1970
Spot, Leiostomus xanthurus	whole body	1.1**	2,300	35	Parrish, et al. 1973

---

* Converted from dry to wet weight basis

**Data for % lipid from Hansen, 1980

Maximum Permissible Tissue Concentration

Action Level or Effect	Concentration (mg/kg)	Reference
Fish and shellfish	0.3	U.S. FDA Guideline 7420.08, 1978
Fish oil	0.3	U.S. FDA Guideline 7426.04, 1977
Altered ammonia detoxifying mechanism of rainbow trout, Salmo gairdneri	0.36 of diet	Mehrle & Bloomfield, 1974
Altered phenylalanine mechanism of rainbow trout, Salmo gairdneri	0.36 of diet	Mehrle & DeClue, 1972

Table 5. **(Continued)**

Geometric mean of normalized BCF values (see text) = 1,557

Marketability for human consumption: FDA action level for fish and shellfish = 0.3 mg/kg

Percent lipid values for freshwater species (see Guidelines) = 15

Percent lipid value for saltwater species (see Guidelines) = 16

Freshwater: $\frac{0.3}{1,557 \times 15} = 0.000013$ mg/kg = 0.013 µg/l

Saltwater: $\frac{0.3}{1,557 \times 16} = 0.000012$ mg/kg = 0.012 µg/l

Using highest BCF for edible portion of a consumed species

Freshwater: Channel catfish = 2,993 (Shannon, 1977a)

$\frac{0.3}{2,993} = 0.00010$ mg/kg = 0.10 µg/l

Saltwater: Eastern oyster = 8,000 (Parrish, 1974)

$\frac{0.3}{8,000} = 0.000038$ mg/kg = 0.038 µg/l

FDA action level for fish oil = 0.3 mg/kg

Percent lipid value for fish oil = 100

Freshwater and Saltwater: $\frac{0.3}{1,557 \times 100} = 0.0000019$ mg/kg = 0.0019 µg/l

Freshwater Final Residue Value = 0.0019 µg/l

Saltwater Final Residue Value = 0.0019 µg/l

Table 6. Other data for aldrin/dieldrin

Species	Chemical	Duration	Effect	Result (µg/l)	Reference
		FRESHWATER SPECIES			
Amoeba, *Acanthamoeba castellanii*	Dieldrin	6 days	No effect on survival	10,000	Prescott, et al. 1977
Tubificids (mixture), *Tubifex* and *Limnodrilus*	Dieldrin	96 hrs	LC50	6,700	Whitten & Goodnight, 1966
Ostracod, *Cypretta kawatai*	Dieldrin	24 hrs	LC50	185	Hansen & Kawatski, 1976
Ostracod, *Cypretta kawatai*	Dieldrin	72 hrs	LC50	12.3	Hansen & Kawatski, 1976
Aquatic insects	Dieldrin	6 mos	Bioconcentration in naturally exposed animals	4,620	Bulkley, et al. 1974
Stonefly, *Pteronarcys californica*	Dieldrin	30 days	LC50	2	Jensen & Gaufin, 1966
Stonefly, *Acroneuria pacifica*	Dieldrin	30 days	LC50	0.2	Jensen & Gaufin, 1966
Midge, *Chironomus tentans*	Dieldrin	24 hrs	LC50	0.9	Karnak & Collins, 1974
Rainbow trout, *Salmo gairdneri*	Dieldrin	17-23 days	Lethal muscle tissue concentration 7.7 mg/kg	2.3	Holden, 1966
Rainbow trout, *Salmo gairdneri*	Dieldrin	140 days	Altered concentrations of 11 amino acids	1 mg/kg/wk	Mehrle, et al. 1971
Rainbow trout, *Salmo gairdneri*	Dieldrin	140 days	Increased lipid	0.2 mg/kg/wk	Macek, et al. 1970
Rainbow trout, *Salmo gairdneri*	Dieldrin	168 days	Equilibrium bioaccumulation of 1.05 mg/kg	0.2 mg/kg/wk	Macek, et al. 1970

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result (µg/l)	Reference
Carp, *Cyprinus carpio*	Dieldrin	96 hrs	100% mortality of embryos	5,000	Malone & Blaylock, 1970
Channel catfish, *Ictalurus punctatus*	Dieldrin	210 days	Reduced growth	4 µg/g of diet (dry wt.)	Argyle, 1975
Black bullhead, *Ictalurus melas*	Dieldrin	36 hrs	LC50	2.5	Ferguson, et al. 1965
Mosquitofish, *Gambusia affinis*	Dieldrin	48 hrs	LC50	8	Culley & Ferguson, 1969
Green sunfish, *Lepomis cyanellus*	Dieldrin	111 hrs	Concentration in blood at death	5.65 µg/g	Hogan & Roelofs, 1971
Green sunfish, *Lepomis cyanellus*	Dieldrin	111 hrs	Concentration in brain at death	10.31 µg/g	Hogan & Roelofs, 1971
Walleye, *Stizostedion vitreum*	Dieldrin	embryonic stage of develop.	Behavioral aberrations of yolk sac fry	12.2	Hair, 1972
Toad (tadpoles), *Bufo woodhousi*	Dieldrin	96 hrs	LC50	150	Sanders, 1970
Frog (tadpoles), *Pseudacris triseriata*	Dieldrin	96 hrs	LC50	100	Sanders, 1970
Amoeba, *Acanthamoeba castellanii*	Aldrin	6 days	No effect on survival	10,000	Prescott, et al. 1977
Cladoceran, *Daphnia magna*	Aldrin	3 days	Bioconcentration	14,100	Johnson, et al. 1971
Mayfly, *Hexagenia bilineata*	Aldrin	3 days	Bioconcentration	6,300	Johnson, et al. 1971
Stonefly, *Pteronarcys californica*	Aldrin	30 days	LC50	2.5	Jensen & Gaufin, 1966

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result (µg/l)	Reference
Stonefly, *Aeroneuria pacifica*	Aldrin	30 days	LC50	22	Jensen & Gaufin, 1966
Midge, *Chironomus* sp.	Aldrin	3 days	Bioconcentration	4,600	Johnson, et al. 1971
Carp, *Cyprinus carpio*	Aldrin	-	Significant increase of sodium in perfused gill	180	McBride & Richards, 1975
Black bullhead, *Ictalurus melas*	Aldrin	36 hrs	LC50	12.5	Ferguson, et al. 1965
Mosquitofish, *Gambusia affinis*	Aldrin	48 hrs	LC50	36	Culley & Ferguson, 1969
Mosquitofish, *Gambusia affinis*	Aldrin	24 hrs	LC50	270	Krieger & Lee, 1973
Bluegill, *Lepomis macrochirus*	Aldrin	-	50% inhibition dose of Na^+-K^+ ATPase	30 µM	Yap, et al. 1975
Toad (tadpoles), *Bufo woodhousii*	Aldrin	96 hrs	LC50	150	Sanders, 1970
		SALTWATER SPECIES			
Alga, *Skeletonema costatum*	Dieldrin	2 hrs	Bioconcentration factor = 1,588*	-	Rice & Sikka, 1973
Alga, *Tetraselmis chuii*	Dieldrin	2 hrs	Bioconcentration factor = 859*	-	Rice & Sikka, 1973
Alga, *Isochrysis galbana*	Dieldrin	2 hrs	Bioconcentration factor = 824*	-	Rice & Sikka, 1973
Alga, *Olisthodiscus luteus*	Dieldrin	2 hrs	Bioconcentration factor = 490*	-	Rice & Sikka, 1973
Alga, *Cyclotella nana*	Dieldrin	2 hrs	Bioconcentration factor = 481*	-	Rice & Sikka, 1973

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result (µg/l)	Reference
Alga, *Amphidinium carteri*	Dieldrin	2 hrs	Bioconcentration factor = 98*	-	Rice & Sikka, 1973
Clam, *Rangia cuneata*	Dieldrin	72 hrs	Bioconcentration factor = 1,600	-	Petrocelli, et al. 1973
Eastern oyster, *Crassostrea virginica*	Dieldrin	7 days	Bioconcentration factor = 2,070	-	Mason & Rowe, 1976
Eastern oyster, *Crassostrea virginica*	Dieldrin	7 days	Bioconcentration factor = 2,880	-	Mason & Rowe, 1976
Eastern oyster, *Crassostrea virginica*	Dieldrin	1 day	EC50	15.0	Lowe, undated
Eastern oyster, *Crassostrea virginica*	Dieldrin	1 day	EC50	240.0	Lowe, undated
Pink shrimp, *Penaeus duorarum*	Dieldrin	2 days	EC50	0.28	Lowe, undated
Brown shrimp, *Penaeus aztecus*	Dieldrin	2 days	EC50	3.2	Lowe, undated
Brown shrimp, *Crangon crangon*	Dieldrin	2 days	LC50	>10, <33	Portmann & Wilson, 1971
Shore crab, *Carcinus maenus*	Dieldrin	2 days	LC50	>10, <33	Portmann & Wilson, 1971
Fiddler crab, *Uca pugilator*	Dieldrin	15 days	Dieldrin in food affected running behavior	0.1 µg/g	Klein & Lincer, 1974
Crab larvae, *Leptodius floridanus*	Dieldrin	18 days	Bioaccumulated after consuming food with 213 µg/kg	217 µg/g	Epifanio, 1973
Crab larvae, *Leptodius floridanus*	Dieldrin	6 days	Approximate LC50	1	Epifanio, 1971
Crab larvae, *Leptodius floridanus*	Dieldrin	16 days	Bioconcentration factor = 7,052	-	Epifanio, 1973

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result (µg/l)	Reference
Blue crab, Callinectes sapidus	Dieldrin	10 days	Bioaccumulated 4 to 7 times the daily dose in food	-	Petrocelli, et al. 1975
Blue crab (juvenile), Callinectes sapidus	Dieldrin	2 days	EC50	23.0	Lowe, undated
Sheepshead minnow, Cyprinodon variegatus	Dieldrin	2 days	LC50	5.82	Wade, 1969
Sheepshead minnow, Cyprinodon variegatus	Dieldrin	2 days	LC50	24.0	Lowe, undated
Sailfin molly, Poecilia latipinna	Dieldrin	2 days	LC50	10.8	Wade, 1969
Sailfin molly, Poecilia latipinna	Dieldrin	34 wks	LC50	>1.5, <3.0	Lane & Livingston, 1970
Spot, Leiostomus xanthurus	Dieldrin	1 day	LC50	3.2	Lowe, undated
White mullet, Mugil curema	Dieldrin	2 days	LC50	7.1	Butler, 1963
Striped mullet, Mugil cephalus	Dieldrin	2 days	LC50	3.2	Lowe, undated
Striped mullet, Mugil cephalus	Dieldrin	2 days	LC50	3.2	Lowe, undated
Striped mullet, Mugil cephalus	Dieldrin	2 days	LC50	0.66	Lowe, undated
Winter flounder, Pseudopleuronectes americanus	Dieldrin	-	1.21 mg/kg in embryos caused 88% reduction in fertilization	-	Smith & Cole, 1973
Pink shrimp, Penaeus duorarum	Aldrin	1 day	EC50	0.37	Lowe, undated

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result (µg/l)	Reference
Blue crab (juvenile), *Callinectes sapidus*	Aldrin	2 days	EC50	23	Lowe, undated
Spot, *Leiostomus xanthurus*	Aldrin	2 days	LC50	3.2	Lowe, undated
White mullet, *Mugil curema*	Aldrin	2 days	LC50	2.8	Butler, 1963
Striped mullet, *Mugil cephalus*	Aldrin	2 days	LC50	2.0	Lowe, undated

---

* Correction factor (0.1) for dry weight analysis

REFERENCES

Adema, D.M.M. 1978. *Daphnia magna* as a test animal in acute and chronic toxicity tests. Hydrobiol. 59: 125.

Argyle, R.L., et al. 1975. Dieldrin in the diet of channel catfish (*Ictalurus punctatus*): Uptake and effect on growth. Jour. Fish. Res. Board Can. 32: 2197.

Batterton, J.C., et al. 1971. Growth response of bluegreen algae to aldrin, dieldrin, endrin and their metabolites. Bull. Environ. Contam. Toxicol. 6: 589.

Bedford, J.W. and M.J. Zabik. 1973. Bioactive compounds in the aquatic environment: Uptake and loss of DDT and dieldrin by freshwater mussels. Arch. Environ. Contam. Toxicol. 1: 97.

Bulkley, R.V., et al. 1974. Contamination of channel catfish with dieldrin from agricultural runoff. Completion Report, Iowa Water Resour. Res. Inst., Ames. No. 62, PB-236 416, Natl. Tech. Inf. Serv., Springfield, Virginia.

Butler, P.A. 1963. Commercial Fisheries Investigations. *In*: Pesticide and Wildlife Studies: A Review of Fish and Wildlife Service Investigations During 1961 and 1962. U.S. Fish Wildl. Serv. Circ. 167: 11.

Cairns, J., Jr. 1968. The effects of dieldrin on diatoms. Mosq. News. 28: 177.

Cairns, J., Jr. and J.J. Loos. 1966. Changes in guppy populations resulting from exposure to dieldrin. Prog. Fish Cult. 28: 220.

Chadwick, G.G. and U. Kiigemagi. 1968. Toxicity evaluation of a technique for introducing dieldrin into water. Jour. Water Pollut. Control Fed. 40: 76.

Chadwick, G.G. and D.L. Shumway. 1969. Effects of Dieldrin on the Growth and Development of Steelhead Trout. In: The Biological Impact of Pesticides in the Environment. Environ. Health Sci. Ser. No. 1, Oregon St. Univ. p. 90.

Culley, D.D. and D.E. Ferguson. 1969. Patterns of insecticide resistance in the mosquito fish Gambusia affinis. Jour. Fish. Res. Board Can. 26: 2395.

Earnest, R.D. and P.E. Benville, Jr. 1972. Acute toxicity of four organochlorine insecticides to two species of surf perch. Calif. Fish Game. 58: 127.

Eisler, R. 1969. Acute toxicities of insecticides to marine decapod crustaceans. Crustaceana. 16: 302.

Eisler, R. 1970a. Factors affecting pesticide-induced toxicity in an estuarine fish. U.S. Bureau Sport Fish. Wildl., Tech. Paper 45.

Eisler, R. 1970b. Acute toxicities of organochlorine and organophosphorus insecticides to estuarine fishes. U.S. Bur. Sport Fish. Wildl., Tech. Pap. 46.

Epifanio, C.E. 1971. Effects of dieldrin in seawater on the development of two species of crab larvae, _Leptodius floridanus_ and _Panopeus herbstii_. Mar. Biol. 11: 356.

Epifanio, C.E. 1973. Dieldrin uptake by larvae of the crab _Leptodius floridanus_. Mar. Biol. 19: 320.

Ferguson, D.E., et al. 1965. Tolerance to five chlorinated hydrocarbon insecticides in two species of fish from a transect of the lower Mississippi River. Jour. Miss. Acad. Sci. 11: 239.

Gaufin, A.R., et al. 1965. The toxicity of ten organic insecticides to various aquatic invertebrates. Water Sewage Works. 12: 276.

Hair, E.M. 1972. Effects of dieldrin on walleye egg development, hatching and fry survival. Thesis, Ohio State Univ., Columbus, Ohio.

Hansen, C.R., Jr. and J.A. Kawatski. 1976. Application of 24-hour post-exposure observation to acute toxicity studies with invertebrates. Jour. Fish. Res. Board Can. 33: 1198.

Hansen, D. 1980. Memorandum to C.E. Stephan. U.S. Environ. Prot. Agency. August.

Henderson, C., et al. 1959. Relative toxicity of ten chlorinated hydrocarbon insecticides to four species of fish. Trans. Am. Fish. Soc. 88: 23.

Hogan, R.L. and E.W. Roelofs. 1971. Concentrations of dieldrin in the blood and brain of the green sunfish, *Lepomis cyanellus*, at death. Jour. Fish Res. Board Can. 28: 610.

Holden, A.W. 1966. Organochlorine insecticide residues in salmonid fish. Jour. Appl. Ecol. 3(Suppl.): 45.

Jensen, L.D. and A.R. Gaufin. 1964. Effects of ten organic insecticides on two species of stonefly naiads. Trans. Am. Fish. Soc. 93: 27.

Jensen, L.D. and A.R. Gaufin. 1966. Acute and long-term effects of organic insecticides on two species of stonefly naiads. Jour. Water Pollut. Control Fed. 38: 1273.

Johnson, B.T., et al. 1971. Biological magnification and degradation of DDT and aldrin by freshwater invertebrates. Jour. Fish. Res. Board Can. 28: 705.

Karnak, R.E. and W.J. Collins. 1974. The susceptibility to selected insecticides and acetylcholinesterase activity in a laboratory colony of midge larvae, *Chironomus tentans*. Bull. Environ. Contam. Toxicol. 12: 62.

Katz, M. 1961. Acute toxicity of some organic insecticides to three species of salmonids and to the threespine stickleback. Trans. Am. Fish. Soc. 90: 264.

Klein, M.L. and J.L. Lincer. 1974. Behavioral Effects of Dieldrin upon the Fiddler Crab, *Uca pugilator*. *In*: J. Vernberg and W.B. Vernberg (eds.), Pollution and Physiology of Marine Organisms. Academic Press, New York. p. 181.

Korn, S. and R. Earnest. 1974. Acute toxicity of twenty insecticides to striped bass, *Morone saxatilis*. Calif. Fish Game. 60: 128.

Krieger, R.I. and P.W. Lee. 1973. Inhibition of *in vivo* and *in vitro* epoxi- dation of aldrin, and potentiation of toxicity of various insecticide chemi- cals by Diquat in two species of fish. Arch. Environ. Contam. Toxicol. 1: 112.

Lane, C.E. and R.J. Livingston. 1970. Some acute and chronic effects of dieldrin on the sailfin molly, *Poecilia latipinna*. Trans. Am. Fish. Soc. 99: 489.

Lowe, J.I. Results of toxicity tests with fishes and macroinvertebrates. Data sheets available from U.S. Environmental Protection Agency, Environmental Research Laboratory, Gulf Breeze, Florida. 32561.

Macek, K.J., et al. 1969. The effects of temperature on the susceptibility of bluegills and rainbow trout to selected pesticides. Bull. Environ. Contam. Toxicol. 4: 175.

Macek, K.J., et al. 1970. The uptake, distribution and elimination of dietary ^{14}C-DDT and ^{14}C-Dieldrin in rainbow trout. Trans. Am. Fish. Soc. 99: 689.

Malone, C.R. and B.G. Blaylock. 1970. Toxicity of insecticide formulations to carp embryos reared in vitro. Jour. Wildl. Manage. 34: 460.

Mason, J.W. and R. Rowe. 1976. The accumulation and loss of dieldrin and endrin in the eastern oyster. Arch. Environ. Contam. Toxicol. 4: 349.

McBride, R.K. and B.D. Richards. 1975. The effects of some herbicides and pesticides on sodium uptake by isolated perfused gills from the carp *Cyprinus carpio*. Comp. Biochem. Physiol. 51C: 105.

Mehrle, P.M. and R.A. Bloomfield. 1974. Ammonia detoxifying mechanisms of rainbow trout altered by dietary dieldrin. Toxicol. Appl. Pharmacol. 27: 355.

Mehrle, P.M. and M.E. DeClue. 1972. Phenylalamine metabolism altered by dietary dieldrin. Nature. 238: 462.

Mehrle, P.M., et al. 1971. Serum amino acids in rainbow trout (*Salmo gairdneri*) as affected by DDT and dieldrin. Comp. Biochem. Physiol. 38B: 373.

Parrish, P.R. 1974. Aroclor 1254, DDT and DDD, and dieldrin: Accumulation and loss by American oysters (*Crassostrea virginica*) exposed continuously for 56 weeks. Proc. Natl. Shellfish. Assoc. 64(7).

Parrish, P.R., et al. 1973. Dieldrin: Effects on Several Estuarine Organisms. *In*: Proc. 27th Annu. Conf. S.E. Assoc. Game Fish Comm. p. 427.

Petrocelli, S.R., et al. 1973. Uptake and accumulation of an organochlorine insecticide (dieldrin) by an estuarine mollusc, *Rangia cuneata*. Bull. Environ. Contam. Toxicol. 10: 315.

Petrocelli, S.R., et al. 1975. Biomagnification of dieldrin residues by food-chain transfer from clams to blue crabs under controlled conditions. Bull. Environ. Contam. Toxicol. 13: 108.

Portmann, J.E. and K.W. Wilson. 1971. The Toxicity of 140 Substances to the Brown Shrimp and other Marine Animals. *In*: Shellfish Information Leaflet #22. Ministry of Agriculture, Fisheries and Food. Fisheries Lab. Burnham-on-Crouch, Essex. p. 1.

Prescott, L.M., et al. 1977. The effects of pesticides, polychlorinated biphenyls and metals on the growth and reproduction of *Acanthamoeba castellanii*. Bull. Environ. Contam. Toxicol. 18: 29.

Rehwoldt, R.E., et al. 1977. Investigations into acute toxicity and some chronic effects of selected herbicides and pesticides on several freshwater fish species. Bull. Environ. Contam. Toxicol. 18: 361.

Reinert, R.E. 1972. Accumulation of dieldrin in an alga (*Scenedesmus obliqus*), *Daphnia magna* and the guppy (*Poecilia reticulata*). Jour. Fish. Res. Board Can. 29: 1413.

Reinert, R.E., et al. 1974. Dieldrin and DDT: Accumulation from water and food by lake trout (*Salvelinus namaycush*) in the laboratory. Proc. 17th Conf. Great Lakes Res. 52.

Rice, C.P. and H.C. Sikka. 1973. Fate of dieldrin in selected species of marine algae. Bull. Environ. Contam. Toxicol. 9: 116.

Roelofs, T.D. 1971. Effects of dieldrin on the intrinsic rate of increase of the guppy *Poecilia reticulata* Peters. Thesis, Oregon State Univ., Corvallis, Oregon.

Rose, F.L. and C.D. McIntire. 1970. Accumulation of dieldrin by benthic algae in laboratory streams. Hydrobiol. 35: 481.

Sanders, H.O. 1969. Toxicity of pesticides to the crustacean, *Gammarus lacustris*. Bur. Sport Fish. Wildl. Tech. Pap. No. 25.

Sanders, H.O. 1970. Pesticide toxicities to tadpoles of the western chorus frog *Pseudacris triseriata* and Fowler's toad *Bufo woodhousii fowleri*. Copeia. 2: 246.

Sanders, H.O. 1972. Toxicity of some insecticides to four species of malacostracan crustaceans. Bur. Sport Fish. Wildl. Tech. Pap. No. 66.

Sanders, H.O. and O.B. Cope. 1966. Toxicities of several pesticides to two species of cladocerans. Trans. Am. Fish. Soc. 95: 165.

Santharam, K.R., et al. 1976. Toxicity of some insecticides to *Daphnia carinata* King, an important link in the food chain in the freshwater ecosystems. Ind. Jour. Ecol. 3: 70.

Schoettger, R.A. 1970. Fish-Pesticide Research Laboratory, Progress in Sport Fishery Research. U.S. Dept. Int., Bur. Sport Fish Wildl. Res. Publ. 106.

Shannon, L.R. 1977a. Accumulation and elimination of dieldrin in muscle tissue of channel catfish. Bull. Environ. Contam. Toxicol. 17: 637.

Shannon, L.R. 1977b. Equilibrium between uptake and elimination of dieldrin by channel catfish, Ictalurus punctatus. Bull. Environ. Contam. Toxicol. 17: 278.

Smith, R.M. and C.F. Cole. 1973. Effects of egg concentrations of DDT and dieldrin on development in winter flounder (Pseudopleuronectes americanus). Jour. Fish. Res. Board. Can. 30: 1894.

Stadnyk, L. and R.S. Campbell. 1971. Pesticide effect on growth and ^{14}C assimilation in freshwater alga. Bull. Environ. Contam. Toxicol. 6: 1.

Tarzwell, C.M. and C. Henderson. 1957. Toxicity of dieldrin to fish. Trans. Am. Fish. Soc. 86: 245.

U.S. EPA. 1980. Unpublished laboratory data. Environ. Res. Lab., Gulf Breeze, Florida. 32561.

U.S. Food and Drug Administration. 1977. Administrative Guideline 7426.04, Attachment A, July 29.

U.S. Food and Drug Administration. 1978. Administrative Guideline 7420.08, Attachment A, October 5.

Wade, R.A. 1969. Ecology of juvenile tarpon and effects of dieldrin on two associated species. U.S. Bur. Sport Fish. Wildl. Tech. Paper 41.

Whitten, B.K. and C.J. Goodnight. 1966. Toxicity of some common insecticides to tubificids. Jour. Water Pollut. Control Fed. 38: 227.

Worthley, E.G. and C.D. Schott. 1971. The comparative effects of CS and various pollutants on freshwater phytoplankton colonies of *Wolffia papulifera* Thompson. Dept. of Army, Edgewood Arsenal Biomed. Lab. Task IW662710-AD6302.

Yap, H.H., et al. 1975. *In vitro* inhibition of fish brain ATPase activity by cyclodiene insecticides and related compounds. Bull. Environ. Contam. Toxicol. 14: 163.

Mammalian Toxicology and Human Health Effects

INTRODUCTION

During the past decade, considerable information has been generated concerning the toxicity and potential carcinogenicity of the two organochlorine pesticides aldrin and dieldrin. These two pesticides are usually considered together since aldrin is readily expoxidized to dieldrin in the environment. Both are acutely toxic to most forms of life including arthropods, mollusks, invertebrates, amiphibians, reptiles, fish, birds, and mammals. Dieldrin is extremely persistent in the environment. By means of bioaccummulation it is concentrated manyfold as it moves up the food chain.

Aldrin and dieldrin are manmade compounds belonging to the group of cyclodiene insecticides. They are a sub-group of the chlorinated cyclic hydrocarbon insecticides which include DDT, BHC, etc. They were manufactured in the United States by Shell Chemical Company until the U.S. EPA prohibited their manufacture in 1974 (39 FR 37246) under the Federal Insecticide, Fungicide and Rodenticide Act. They are currently manufactured by Shell Chemical Company in Holland. Prior to 1974, both insecticides were available in the United States in various formulations for broad-spectrum insect control. They were used for control of soil pests and grasshoppers, protection of vegetables and fruits, and control of disease vectors including locusts and termites (Int. Agency Res. Cancer, 1974a,b). In 1974, the U.S. EPA restricted the use of aldrin/dieldrin to termite control by direct soil injection and nonfood seed and plant treatment.

Early work by Treon and Cleveland (1955) suggested that aldrin and dieldrin may have tumor-inducing potential, especially in the liver. Since that time, several conflicting reports of the hepatocarcinogenicity in mice, rats, and dogs have appeared in literature. Studies have been carried out mainly by the U.S. Food and Drug Administration, the National Cancer Institute (NCI), and by the manufacturer, Shell Chemical Company. There has been much debate over the type and significance of hepatic damage caused by aldrin and dieldrin. In order to ascertain the human risks associated with aldrin and dieldrin, evaluations of the toxic effects of these pesticides have been carried out on workers in the Shell Chemical Company. The evaluations include epidemiological studies in addition to the more routine toxicity studies. However, it is felt that the number of workers with high exposures was too small and the time interval too short to determine whether or not aldrin and dieldrin represent a cancer threat to humans.

The objective of this report is to examine published studies so as to utilize the most relevant data to develop a criterion for human risk assessment.

EXPOSURE

Exposure to aldrin and dieldrin is from contaminated waters, food products, and air. Because of its persistence, dieldrin has become widespread in the aquatic environment. It is also spread great distances by wind. Since aldrin and dieldrin are used throughout much of the world beyond the United States, it must be assumed that imported food stuffs, such as meat products, contain residues of these pesticides.

[redacted] of aldrin and dieldrin peaked at 19.3 million lbs. in 1966, and 3.6 million in 1956, respectively (39 FR 37251). The subsequent decline in dieldrin use was due, in part, to increased resistance of boll weevils to chlorinated insecticides (Table 1). The use of dieldrin was preferred to aldrin because it required less application due to its persistence.

Ingestion from Water

Aldrin and dieldrin have been applied to vast areas of agricultural land and aquatic areas in the United States and in most parts of the world. These pesticides have therefore found their way into most fresh and marine waters. Unlike DDT, aldrin and dieldrin are somewhat more soluble in water (27 and 186 mg/l, respectively) (Park and Bruce, 1968). Gunther, et al. (1968) reported dieldrin to be slightly more soluble at 250 mg/l.

In early studies (Weaver, et al. 1965), dieldrin was found in all major river basins (mean concentration 7.5 ng/l) in the United States and it was found more often than any other pesticide. It was also found in the Mississippi delta (U.S. Dep. Agric., 1966) at 10.0 ng/l while aldrin was found as high as 30 ng/l. Marigold and Schulze (1969) reported aldrin and dieldrin at 40 and 70 ng/l, respectively, in streams in the western United States. Leichtenberg, et al. (1970) found levels of dieldrin and aldrin as high as 114 and 407 ng/l, respectively, in surface waters in the United States.

More recently, dieldrin has been reported to be present in many fresh waters in the United States with mean concentrations

TABLE 1

Domestic Sales of Aldrin and Dieldrin From 1950 Through July 1, 1974[*]

Year	Aldrin (1,000 lbs)	Dieldrin (1,000 lbs)
1950	1,456	0
1951	3,288	185
1952	814	750
1953	1,234	1,135
1954	2,993	1,777
1955	4,372	2,585
1956	6,495	8,635
1957	2,431	2,673
1958	4,971	3,074
1959	5,566	3,008
1960	8,109	2,650
1961	9,926	2,764
1962	10,886	2,990
1963	12,152	2,685
1964	12,693	2,052
1965	14,278	1,814
1966	19,327	1,908
1967	18,092	1,478
1968	13,690	1,332
1969	9,902	1,206
1970	8,909	749
1971	11,615	705
1972	11,868	740
1973 (to July 1)	8,721	432
1973 estimated (to Dec. 31)	(10,000)	(576)
1973	9,900	------
1974 (to July 1)	9,700	------

---

[*] Source: 39 FR, 1974

ranging from 5 to 395 ng/l in surface water and from 1 to 7 µg/l in drinking water (Epstein, 1976).

In 1975 a survey in the United States of aldrin, dieldrin, DDT, and DDT metabolite levels in raw and drinking water was carried out (U.S. EPA, 1976). Dieldrin was found in 117 of 715 samples analyzed (Table 2). The six samples in the highest range were all taken from the same location, three from raw waters and three from finished waters. Three of these six samples also contained aldrin in concentration of 15 to 18 ng/l.

Harris, et al. (1977) summarized the distribution of various chemicals in drinking water in several cities in the United States. Dieldrin was found in concentrations of 1 ng/l in Seattle, Washington, and Cincinnati, Ohio; 2 ng/l in Miami, Florida, and Ottumwa, Iowa; and as high as 50 ng/l in New Orleans, Louisiana.

It has been estimated (MacKay and Wolkoff, 1973) that unlike many chlorinated hydrocarbons that evaporate rapidly from shallow waters, dieldrin has by far the longest half-life of these compounds in water 1 meter in depth. They calculated that the half-life for aldrin and dieldrin would be 10.1 days and 723 days, respectively, compared to 3.5 days for DDT and 289 days for lindane. This long half-life in water combined with the potential for bioconcentration by aquatic organisms such as microorganisms, phytoplankton, mollusks, and fish further enhances the hazard of these two pesticides (Wurster, 1971).

Ingestion from Food

Although aldrin is readily converted to dieldrin, dieldrin itself is stable and persistent in the environment. Because it is

TABLE 2

Dieldrin Concentrations in Raw and Drinking Water*

No. of Samples	598	94	13	4	6
ng/l	4	4-10	11-20	21-29	56-110

*Source: U.S. EPA, 1976

lipophilic, dieldrin accumulates in the food chain (Wurster, 1971). The persistence of aldrin and dieldrin in different soils varies with the type of soil and with movement to other areas by water, wind, etc. (Matsumura and Boush, 1967). Dieldrin has been shown to be one of the most persistent of all the organochlorine pesticides (Nash and Woolson, 1967).

It has been estimated that 99.5 percent of all human beings in the United States have dieldrin residues in their tissues (U.S. EPA, 1971). Although there are other origins of contamination, these residue levels are mainly due to contamination of foods of animal origin (Wurster, 1971). The levels of aldrin/dieldrin in several types of food have been summarized by Edwards (1973), Matsumura (1974), and Manske and Johnson (1975). The overall concentration of dieldrin in the diet in the United States has been calculated to be approximately 43 ng/g of food consumed (Epstein, 1976). Table 3 lists the estimated daily dietary intake for aldrin and dieldrin of a late teen-aged male (National Academy of Sciences (NAS), 1975).

A bioconcentration factor (BCF) relates the concentration of a chemical in aquatic animals to the concentration in the water in which they live. The steady-state BCFs for a lipid-soluble compound in the tissues of various aquatic animals seem to be proportional to the percent lipid in the tissue. Thus, the per capita ingestion of a lipid-soluble chemical can be estimated from the per capita consumption of fish and shellfish, the weighted average percent lipids of consumed fish and shellfish, and a steady-state BCF for the chemical.

TABLE 3

Estimated Daily Dietary Intake (mg) of a Young Male*

	1965	1966	1967	1968	1969	1970
Aldrin	0.001	0.002	0.001	trace	trace	trace
Dieldrin	0.005	0.007	0.001	0.004	0.005	0.005

*Source: NAS, 1975

Data from a recent survey on fish and shellfish consumption in the United States were analyzed by SRI International (U.S. EPA, 1980). These data were used to estimate that the per capita consumption of freshwater and estuarine fish and shellfish in the United States is 6.5 g/day (Stephan, 1980). In addition, these data were used with data on the fat content of the edible portion of the same species to estimate that the weighted average percent lipids for consumed freshwater and estuarine fish and shellfish is 3.0 percent.

Two laboratory studies, in which percent lipids and a steady-state BCF were measured, have been conducted on dieldrin. The mean of the BCF values, after normalization to one percent lipids, is 1,557 (see Table 5 in Section B). An adjustment factor of 3 can be used to adjust the mean normalized BCF to the 3.0 percent lipids that is the weighted average for consumed fish and shellfish. Thus, the weighted average bioconcentration factor for dieldrin and the edible portion of all freshwater and estuarine aquatic organisms consumed by Americans is calculated to be 4,670.

No useful measured bioconcentration factor can be obtained for aldrin because it is rapidly converted to dieldrin by aquatic organisms. In addition, because aldrin is converted to dieldrin in soil, aquatic organisms are rarely exposed to aldrin.

However, the equation "Log BCF = (0.85 Log P) - 0.70" can be used (Veith, et al. 1979) to estimate the BCF for aquatic organisms that contain about 7.6 percent lipids (Veith, 1980) from the octanol-water partition coefficient (P). Based on a measured log P value of 3.01 (Hansch and Leo, 1979), the steady-state bioconcentration factor for aldrin is estimated to be 72. An adjustment factor of 3.0/7.6 = 0.395 can be used to adjust the estimated BCF from the 7.6 percent lipids on which the equation is based to the 3.0 percent lipids that is the weighted average for consumed fish and shellfish. Thus, the weighted average bioconcentration factor for aldrin and the edible portion of all freshwater and estuarine aquatic organisms consumed by Americans is calculated to be 72 x 0.395 = 28.

Inhalation

Aldrin and dieldrin enter the air through various mechanisms such as spraying, wind action, water evaporation, and adhesion to particulates. Stanley, et al. (1971) reported levels of aldrin and dieldrin in air samples in nine cities in the United States. One sample of the air in Iowa City, Iowa had detectable levels of aldrin (8.0 ng/m^3), and 50 samples taken in Orlando, Florida had detectable amounts of dieldrin, the largest being 29.7 ng/m^3. Various other studies of the air carried out during the 1960's were summarized by Edwards (1973).

In a study conducted by the U.S. EPA from 1970 to 1972 (Epstein, 1976), dieldrin was found in more than 85 percent of the air samples tested. The mean levels ranged from 1 to 2.8 ng/m^3. From these levels, the average daily intake of dieldrin by respiration was calculated to be 0.035 to 0.098 µg.

Although aldrin/dieldrin are no longer used in the United States, there is still the possibility of air borne contamination from other parts of the world. Edwards (1973) showed that dieldrin has been transported long distances in the air. Exposure due to inhalation of aldrin and dieldrin from the application of these pesticides was, of course, much greater before the restriction of their use. Pesticide applicators and individuals living near agricultural areas were exposed to aldrin/dieldrin through inhalation.

In a recent report, Domanski, et al. (1977) reported no increase in dieldrin concentration in adipose tissue of cigarette smokers as compared to nonsmokers although tobacco has high residues of pesticides and is stored many years before use.

Dermal

Dermal exposure to aldrin or dieldrin is limited to those involved in manufacturing or application of these pesticides. Wolfe, et al. (1972) reported that exposure to workers, both manufacturers and applicators, was mainly through dermal absorption rather than from inhalation. Due to the ban on manufacturing of the pesticides in the United States, the possibilities of dermal exposure have been greatly reduced.

PHARMACOKINETICS

Absorption

Heath and Vandekar (1964), using ^{36}Cl-dieldrin (4 percent in arachis oil) showed that absorption by the upper part of the gastroinestinal tract begins almost immediately after oral administration in rats and that the absorption varies with the solvent used. Barnes and Heath (1964) demonstrated that the LD_{50} varies with the dieldrin-to-solvent ratio. Heath and Vandekar (1964) also demonstrated that absorption is by the portal vein and not the thoracic lymph duct. Initially, dieldrin is widespread but within a few hours it is redistributed in favor of the fat. They also stated that following oral treatment at 25 mg/kg, ^{36}Cl-dieldrin could be recovered from the stomach, small intestine, large intestine, and feces after 1 hour.

Distribution

It is well known that dieldrin has a low solubility in water and a high solubility in fat. At 1 and 2 hours after treatment, Heath and Vandekar (1964) detected the highest concentration of ^{36}Cl-dieldrin in fat tissue. They also reported high concentrations in the liver and kidney with moderate concentrations in the brain at these times.

Deichmann, et al.(1968) studied the retention of dieldrin in blood, liver, and fat. Female Osborne-Mendel rats were fed a diet containing 50 mg/kg dieldrin (87 percent purity). The rats were killed on various days of feeding up to 183 days. The concentration of dieldrin in the blood and liver increased for nine days and then leveled off until the end of the six-month period. The concentration of dieldrin in the fat took approximately 16 days to reach a level that was maintained throughout the experiment. The fat had the highest concentrations of dieldrin followed by the liver. The mean concentration in the fat was 474 times that in the blood, while the concentration in the liver was approximately 29 times the blood concentration.

Walker, et al. (1969) studied the distribution of dieldrin in rats and dogs over a two-year period. Dieldrin (99 percent purity) was incorporated into the diet of CFE male and female rats at 0.1, 1.0, and 10 mg/kg and was fed to dogs in gelatin capsules at concentrations equivalent to 0.1 and 1.0 mg/kg of their daily dietary intake. The authors measured the dieldrin residues in whole blood, fat, liver, and brain and found significantly increased concentrations in all tissues compared to those in the controls (Table 4).

The concentrations in the tissues increased with an increase in the dietary concentrations, and the concentrations in the female rats were considerably higher than those in the males. The dieldrin concentrations reached a plateau by the end of the 6th month and remained fairly constant for the remaining 18 months.

In dogs, the blood concentrations increased in both treatment groups during the first 12 weeks. With the higher dose (1.0 mg/kg/diet) the concentration leveled off between 18 and 30 weeks of treatment. However, with the lower dose (0.1 mg/kg/diet) the plateau was reached between 12 and 18 weeks. In the group receiving 1.0 mg/kg/diet the dieldrin concentration in the blood increased significantly during the final 6 weeks of exposure. The dieldrin concentrations in the liver and brain were also dose-related but, as opposed to the results from the rats, showed no significant sex differences. As in other studies, the concentration in the fat was much greater than that in the liver, which in turn, was greater than in the brain.

Additional studies on the distribution of dieldrin were carried out by Robinson, et al. (1969). In this study Carworth rats were fed dieldrin (99+ percent purity) at 10 mg/kg of their diet for 8 weeks. At the end of this time, they were returned to a dieldrin-free diet and killed randomly in pairs up to 12 weeks after withdrawal of the dieldrin diet. The fatty tissue clearly had the

TABLE 4

Mean Geometric Dieldrin Concentration (μg/g) in Rat Tissues after 104 weeks*

	Dietary Level (mg/kg)	Blood	Fat	Liver	Brain
Males	0	0.0009	0.0598	0.0059	0.0020
	0.1	0.0021	0.02594	0.0159	0.0069
	1.0	0.0312	1.493	0.01552	0.1040
	10.0	0.1472	19.72	1.476	0.4319
Females	0	0.0015	0.3112	0.0112	0.0077
	0.1	0.0065	0.8974	0.0348	0.0224
	1.0	0.0861	13.90	0.4295	0.2891
	10.0	0.3954	57.81	2.965	1.130

*Source: Walker, et al. 1969

highest concentration of dieldrin followed by the liver, brain, and blood. Concentrations of dieldrin in fat returned to control levels after 12 weeks and the decline in dieldrin concentrations was approximately exponential in nature.

Matthews, et al. (1971) investigated the distribution of dieldrin and some of its metabolites in several organs and tissues of both male and female Charles River rats. Three animals of each sex were fasted for eight hours and then given 3 g of food containing 10 mg/kg ^{14}C-dieldrin (96 percent purity). The animals were killed after nine days, and dieldrin and metabolic product concentrations were determined. In general, the amount of radioactivity per gram was higher for the female rats. The kidneys and stomachs of the males contained more radioactivity than those of the females. Levels in the lungs and intestines showed similar differences. The other organs and tissues of the females had three to four times the radioactivity of the males. In the females, storage was predominantly as dieldrin, but in males other metabolites, identified as keto dieldrin, and trans-dihydro-aldrin, and a polar metabolite were detected in various tissues.

Hayes (1974) determined the concentration of dieldrin in the fat, liver, kidney, brain, muscle, and plasma following a single oral dose in rats. Male Sprague-Dawley rats were given 10 mg/kg dieldrin (86 percent purity) by stomach tube. The animals were killed at various intervals up to 240 hours and the dieldrin concentration in the tissues was determined. The concentrations in the brain at 4 and 16 hours were 1.5 and 1.0 µg/g, respectively. Hayes assigned a value of one to the concentrations in the brain and calculated the ratio of the concentrations in other tissues to the concentrations in the brain at 4 and 16 hours (Table 5). The concentrations in the tissues remained relatively constant for 24 hours and began to decline at 48 hours. No further samples were taken until 240 hours when all the dieldrin concentrations were below 0.2 µg/g except the concentration in the fat which was 5 µg/g.

In a study done in 1963 on 30 individuals from three different states, the concentrations of chlorinated hydrocarbon pesticides in body fat were determined (Dale and Quinby, 1963). Twenty-eight individuals were from the general population while one had previous DDT exposure and one had aldrin exposure. The mean (±SE) for the general population was 0.15 ± 0.02 µg/g dieldrin, while that for the aldrin-exposed individual was 0.36 µg/g dieldrin (see discussion on aldrin metabolism to dieldrin in the Metabolism section of this report).

In a study of aldrin and dieldrin concentrations in 71 workers involved in pesticide manufacturing, Hayes and Curley (1968) measured the plasma, fat, and urine concentrations by gas-liquid chromatography. Their findings were in accordance with the earlier animal studies. The fat contained the highest concentration of the pesticides followed by the urine and plasma. The mean concentrations of dieldrin in the fat, urine, and plasma of the pesticide workers were 5.67 ± 1.11, 0.0242 ± 0.0063, and 0.0185 ± 0.0019 µg/g, respectively. These were significantly different from those reported for the general population. The authors reported a high correlation between total hours or intensity of exposure and

TABLE 5

Concentrations of Dieldrin in Tissues of Rats*
(Single Oral Dose)

Hr.	Brain	Muscle	Liver	Kidney	Plasma	Fat
4	1.00 ± 0	0.62 ± 0.05	2.30 ± 0.11	1.55 ± 0.22	0.20 ± 0.02	7.20 ± 1.18
16	1.00 ± 0	0.55 ± 0.06	3.17 ± 0.25	2.02 ± 0.56	1.35 ± 1.11	17.96 ± 3.23

*Source: Hayes, 1974

concentration of dieldrin. However, no correlation could be found between dieldrin concentrations and amount of sick leave.

Another study (Hunter, et al. 1969) involving adult males ingesting 10, 50, or 211 μg dieldrin per day for 18 or 24 months, again found a relationship between the dose and the length of exposure and concentration of dieldrin in the fat and blood. In general, the concentration of dieldrin in the samples increased during the first 18 months and either leveled off or rose slightly during the remaining time. The control and 10 ug groups, both of which were given 211 μg/day for the final 6 months, demonstrated a rise in concentrations similar to the rise demonstrated by those who were given 211 μg/day initially. The authors stated that there was no effect on the general health of the individuals receiving the dieldrin for the two-year test.

In the previously-mentioned studies, blood concentrations of aldrin or dieldrin were determined using whole blood (Deichmann, et al. 1968; Robinson, et al. 1969; Hunter, et al. 1969; Walker, et al. 1969), or plasma (Hayes and Curley, 1968). Mick, et al. (1971) measured the aldrin and dieldrin concentrations in erythrocytes, plasma, and the alpha- and beta-lipoprotein fractions of the blood of six aldrin workers after the workers had formulated 2 million pounds of aldrin over a five-week period. The six workers were exposed to aldrin by both inhalation and dermal contact. The blood samples were collected at the conclusion of the five-week exposure and blood plasma concentrations as high as 312 ng/l were measured. No immediate health problems were reported during this time. In all cases, dieldrin concentrations were higher than the aldrin concentrations due to the epoxidation of aldrin to dieldrin. The dieldrin residue in the plasma averaged approximately four times higher than that in the erythrocytes. As the dieldrin residue in the blood increased, the amount in the plasma became proportionally higher. In addition, the beta-lipoprotein fraction usually contained more dieldrin than the alpha fraction.

The work of Mick, et al. (1971) was confirmed in part by Skalsky and Guthrie (1978). Using labelled pesticides of 98 percent purity incubated with various fractions of human blood *in vitro* Skalsky and Guthrie (1978) were able to demonstrate that dieldrin and DDT bind to albumin and beta-lipoprotein.

Metabolism

Aldrin and its epoxidation product, dieldrin, are both cyclopentadiene insecticides. Since epoxidation of aldrin to dieldrin was first reported by Radomski and Davidow (1953), there have been many reports in the literature of the ability of various organisms (i.e., soil microorganisms, plants, fish, and animals, including man) to epoxidize this type of double bond. Winteringham and Barnes (1955) first reported this reaction with aldrin in mice. Wong and Terriere (1965) were able to demonstrate the *in vitro* conversion of aldrin to its epoxide, dieldrin, using microsomes[1] from male and female rats. The reaction was NADPH-dependent and the enzymes were heat-labile. Winteringham and Barnes (1955) also showed that males converted aldrin to dieldrin at a higher rate. No other metabolic products were detected, although the authors noted that polar products could have been overlooked by the methods used. Nakatsugawa, et al. (1965) confirmed the work of Wong and Terriere (1965) using microsomes from male rats and rabbits. They also demonstrated a requirement for NADPH and stated that dieldrin was not further metabolized by the microsomes. They reported that lung homogenate was only one-tenth as active as liver in epoxidase activity and that no activity was detected in the kidney, spleen, pancreas, heart, or brain.

---

[1] In this document microsomes refers to the cell-free homogenized liver (including soluble enzymes and microsomes) and not to purified microsomes.

Korte (1963) identified one of the metabolic products of aldrin as aldrin diol in studies with rabbits. Heath and Vandekar (1964) reported the existence of a somewhat polar metabolite which is excreted in the feces. They stated that the feces are the main route of excretion and that little dieldrin is excreted unchanged. They were able to detect other polar metabolites in both urine and feces.

Ludwig, et al. (1964) administered ^{14}C-aldrin to male rats at 4.3 µg/day for three months. The compounds excreted into the urine consisted of aldrin, dieldrin, and unidentified hydrophilic metabolic products. These unidentified products made up 75 percent of the dose excreted in the feces and 95 percent excreted in the urine. Two different products were found in the feces and two in the urine. Two of these four products appeared to be identical by paper and thin-layer chromatography.

Korte and Arent (1965) isolated six urinary metabolites from rabbits treated orally with ^{14}C-dieldrin for 21 weeks. The major metabolite (86 percent) was one of the two enantiomorphic isomers of 6,7-trans-dihydroxy-dihydro-aldrin.

Richardson, et al. (1968) were able to identify two metabolites in urine and feces from male CF rats fed a diet containing 100 mg/kg dieldrin for seven months. Metabolites were isolated from the urine and feces collected during the last month. They determined that the urinary metabolite had a keto group on the number 12 carbon and the epoxide was unchanged. The fecal metabolite was a mono-hydroxyderivative of dieldrin at either the 4a or 4 position. A similar study was carried out (Matthews and Matsumura, 1969) in which male rats were fed a diet of 20 mg/kg purified dieldrin for one month, with the dosage increased to 100 mg/kg for 18 days while the urine and feces were collected. Two metabolites were isolated from the feces and two from the urine. The major fecal metabolite was similar to the mono-hydroxy-derivative isolated by Richardson, et al. (1968) in the feces. The major urinary metabolite was identical to the ketone compound identified by Richardson, et al. (1968) in the urine. The minor urinary and fecal metabolites were identical and similar to the 6,7-trans-dihydroxy-dihydro-aldrin described by Korte and Arent (1965).

Matthews and Matsumura (1969) also conducted *in vitro* experiments using ^{14}C-dieldrin incubated with rat liver microsomes and various co-factors. Thin-layer chromatography of the water-soluble components isolated six metabolites in addition to the unchanged dieldrin. Analysis of the water-soluble metabolites revealed a glucuronide conjugate which accounted for approximately 45 percent of the radioactivity. Comparison of the R_F values for the *in vivo* and *in vitro* studies showed that the minor urinary/fecal metabolite (i.e., the 6,7-trans-dihydroxy-dihydro-aldrin) was produced *in* vitro and that the metabolite freed from the glucuronic acid was also present in the in vitro system in the unconjugated form.

The products identified by Richardson, et al. (1968) and Matthews and Matsumura (1969) represent an oxidized form of dieldrin in the urine and feces and a hydroxylated dechlorination metabolite which had lost the intact dieldrin ring system.

Hedde, et al. (1970) were able to isolate six metabolic products in the urine of sheep dosed with ^{14}C-dieldrin. Three castrated sheep were given unlabeled dieldrin orally at 2 mg/kg/day for five days before dosing with ^{14}C-dieldrin. Four other sheep were fed a single oral dose of labeled dieldrin at 20 mg/kg/day. Urine and feces were collected up to six days after treatment with the labeled dieldrin. Although other determinations were made, only the urine was analyzed quantitatively. After hexane extraction at pH 1 followed by other clean-up procedures, the four hexane-soluble metabolites were separated on Sephadex LH-20 gel. The LH-20 was again used to separate the two water soluble metabolites after they were purified by several procedures, including paper chromatography. The authors postulated that these water-soluble metabolites were a glucuronic acid conjugate of the trans-diol and an unidentified conjugate of glucuronic acid and, possibly, glycine.

Feil, et al. (1970) were able to identify two of the hexane-soluble metabolites found by Hedde, et al. (1970) in sheep urine. One was the 6,7-trans-dihydroxy-dihydro-aldrin described by Richardson, et al (1968) and the other was the 9-mono-hydroxy-derivative. Further work on the metabolism of dieldrin (Matthews, et al. (1971) is discussed in the Distribution section of this report where details of treatment are given. Matthews, et al. documented the production of several metabolites of dieldrin including the 6,7-trans-dihydroxy-dihydro-aldrin and a second unidentified polar metabolite excreted in the feces. The mono-hydroxylated compound represented the greatest percentage of the radioactivity extracted from the feces of both male and female rats. In male rats, the chloroform extract of the urine consisted of the keto-metabolite described by Klein, et al. (1968). Also, initially, trans-dihydroxy-dihydro-aldrin was found in the urine of the male rats along with unchanged dieldrin. Most of the radioactivity extracted from the urine of the female rats was in the form of the trans-dihydroxy-dihydro-aldrin, and initially contained up to 20 percent dieldrin.

The metabolism and excretion of dieldrin appears to be more rapid in male than in female rats. Investigators attribute this to the males' ability to produce the more polar metabolites, especially the keto-product which is excreted into the urine.

A recent paper has appeared on the comparative metabolism of dieldrin in rodents. Baldwin, et al. (1972) treated a male CFE rat with 3 mg/kg of ^{14}C-labelled dieldrin and two male CF1 mice with 10 mg/kg. The urine and feces were collected for the following seven or eight days. The authors reported that the CFE rat excreted the pentachloroketone derivative in the urine but that the CF1 mice did not. Conversely, the mice produced an unidentified urinary metabolite which the rat did not. The 6,7-trans-dihydroxy-dihydro-aldrin was found in the feces of the mice and the rat, and a dicarboxylic derivative was found in the urine of all three animals.

A review of the literature on the metabolism of dieldrin and endrin in rodents has been compiled by Bedford and Hutson (1976). They summarized the four known metabolic products of dieldrin as the 6,7-trans-dihydroxy-dihydro-aldrin (trans-diol) and the tricyclic dicarboxylic acid (both of which are products of the transformation of the epoxy group), the syn-12-hydroxy-dieldrin (a monohydro-derivative), and the pentachloroketone.

In comparing dieldrin metabolism in acute or short-term studies versus chronic, low-dose exposure, it must be mentioned that organochlorine compounds, including dieldrin, have been shown to induce the mixed function oxidases (MFO) found in the liver (Kohli, et al. 1977). It is therefore possible, in the long-term animal studies, that investigators have been observing the results of high levels of these enzymes and that the percentages and amounts of certain metabolites may be misleading. Baldwin, et al. (1972) in a limited study, were able to show some inducibility in the CFE male rat but not in the CF1 male mouse. They induced the enzymes by prefeeding the animals for 21 days with low doses (i.e., 10 or 25 mg/kg in diet) of dieldrin. If the results of the Kohli, et al. study are to be accepted, then one may assume that since man is subject to chronic, low-dose exposure to many MFO inducers (including various organochlorine pesticides), this exposure may affect studies of dieldrin metabolism.

Excretion

As mentioned in the Distribution and Metabolism sections of this report, aldrin and/or dieldrin are excreted mainly in the feces and to some extent in the urine in the form of several metabolites that are more polar than the parent compounds. Usually, a plateau is reached in most tissues when the dose is held relatively constant. However, if the dosage increases, the body concentrations will increase and vice versa.

The early work of Ludwig, et al. (1964) demonstrated that male Wistar rats administered daily low doses of ^{14}C-labeled aldrin (4.3 ug for 12 weeks) excreted approximately nine times as much of the radioactivity in the feces as in the urine. After about two weeks of treatment, the rats were excreting 80 percent of the daily dose of aldrin and this increased to 100 percent after eight weeks. Twenty-four hours after the final dose (12 weeks), the animals had excreted 88 percent of the total radioactivity fed. This increased to 98 percent after six weeks and greater than 99 percent after 12 weeks. It appears that after eight weeks of feeding aldrin, a saturation level was attained which did not increase with continued feeding at the same concentration. The concentrations in the body decreased rapidly once the feeding was terminated.

In a study with rabbits administered ^{14}C-dieldrin orally over a 21-week period (total dose 56 to 58 mg/kg), Korte and Arent (1965) reported somewhat conflicting results. At the end of the feeding (22nd week) 42 percent of the total radioactivity had been excreted with two to three times as much in the urine as in the feces. The level in the feces was negligible after 24 weeks while the amount in the urine was up to 43 percent at 52 weeks.

It must be kept in mind that aldrin is metabolized to dieldrin which is then converted to more polar metabolites for excretion. It is possible that the increased amount of radioactivity noted by Korte and Arent (1965) in the feces after treatment with aldrin could be due to the less polar aldrin or dieldrin as compared to the more polar metabolites excreted in the urine or to a basic difference in metabolism of dieldrin in the rabbit.

The work of Robinson, et al. (1969) on the metabolism of dieldrin has been summarized in the Metabolism section of this report. These investigators also studied the loss of dieldrin (99+ percent purity) from the liver, blood, brain, and adipose tissue of male CFE rats fed 10 mg/kg in their diet for eight weeks. Figure 1 illustrates the loss of dieldrin from these tissues. During the period of observation, approximately 99 percent of the dieldrin was excreted at various rates from the tissues. However, it must be noted that the analysis was performed by gas-liquid chromatography and that later investigators (Matthews, et al. 1971) have found liver can contain approximately 30 percent of products other than dieldrin, a fact which may have been overlooked by Robinson, et al. (1969). The fat and brain contained greater than 99 percent of the dieldrin and the excretion times correspond to those for the rat observed by Korte and Arent (1965) in their work six years earlier.

It can be seen from Figure 1 that three of the four slopes for dieldrin loss were not linear and that with the blood and liver, loss was rapid at first and then slowed down. Estimates for the

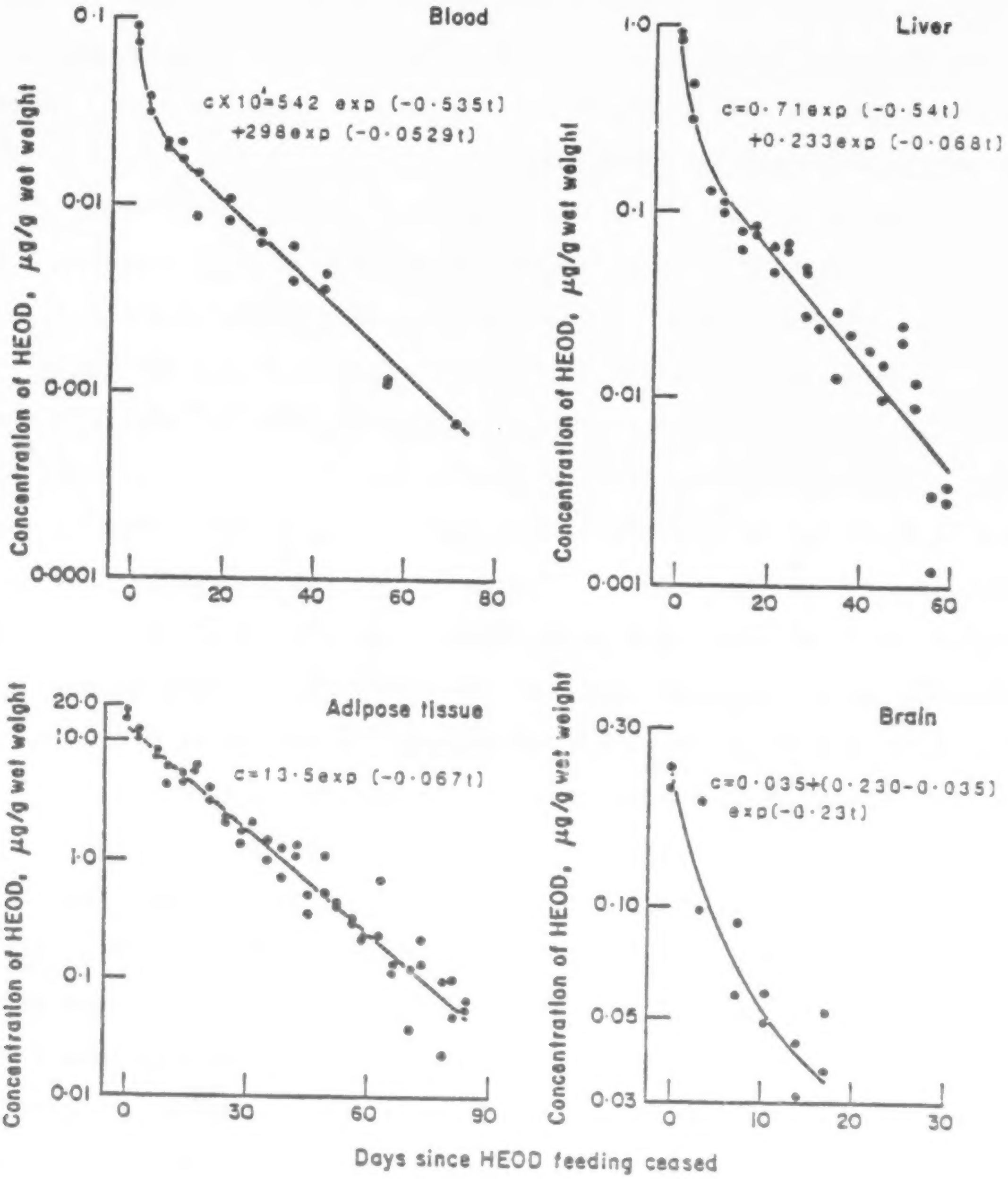

FIGURE 1

The Loss of Dieldrin (HOED) from the Liver,
Blood, Brain, and Adipose Tissue of Male Rats
Source: Robinson, et al. 1969

half-life of dieldrin in the liver and blood were 1.3 days for the period of rapid elimination and 10.2 days for the slower period. The estimated half-life for dieldrin was 10.3 days in the adipose tissue and 3.0 days in the brain.

In the study of ^{14}C-dieldrin metabolism in sheep (Hedde, et al. 1970) mentioned in the Metabolism section of this report, the excretion of dieldrin or its metabolites was higher in the feces than in the urine. This ratio varied considerable due partially to the different doses used. The authors noted that in two very fat sheep the ratio of labelled dieldrin in feces to urine was greater than 10 to 1 but in two thin sheep receiving the same dose, it was slightly greater than 1 to 1. The amount of radioactivity that was exhaled as $^{14}CO_2$ was only 0.25 percent of the total dose. This indicates that virtually none of the dieldrin is broken down to CO_2. With the sheep, less than 50 percent of the total radioactivity was recovered after the five or six days of collection.

Several investigators have shown that removal of dieldrin from the diet results in rapid loss of dieldrin or metabolites from the body, especially the adipose tissue. Barron and Walton (1971) further studied the loss of dieldrin from the body of the rat and also looked at the role of dieldrin in the diet with respect to loss from the adipose tissue. For this study, male Osborne-Mendel rats were fed a diet containing 25 mg/kg dieldrin (99+ percent purity) for 8 weeks. They were then placed on a normal diet and given four daily, oral doses of ^{14}C-dieldrin equivalent to 25 mg/kg in their diet. After these four days, one-half of the animals were then returned to the dieldrin diet (25 mg/kg) while the rest remained on the normal diet. Groups of five animals were sacrificed on the four days when they received the labeled-dieldrin and on days 7, 9, 11, 16, and 23 after the conclusion of the eight-week feeding. The concentration of dieldrin found in the adipose tissue from the rats receiving the dieldrin diet was approximately 50 µg/g and remained at this level throughout the 23 days following the feeding period. The concentrations in the rats on the normal diet decreased to 4 µg/g at day 23. The authors reported that the half-life of dieldrin in the adipose tissue was about 4.5 days, which is somewhat lower than the 10.3 days calculated by Robinson, et al. (1969) with rats fed only 10 mg/kg dieldrin.

Cole, et al. (1970) measured the appearance of ^{14}C-dieldrin and ^{14}C-endrin in the urine and feces of male Holtzman rats for seven days after a single intravenous dose of 0.25 mg/kg of either chemical. They reported that greater than 90 percent of the radioactivity occured in the feces. Approximately 80 percent of the total dose of labeled dieldrin was excreted in the feces after the seven days, compared with approximately 100 percent for the endrin. Cole, et al. (1970) conducted a similar experiment during a four-day period using bile-fistula rats. They also reported that these rats produced a time course of excretion similar to those observed in the first experiment; greater than 90 percent of the excreted radioactivity was found in the bile.

In a comparison of the excretion of dieldrin in the CF1 mouse and CFE rat, Baldwin, et al. (1972) found that after seven or eight days the amount of labelled dieldrin excreted was similar in both species. Also, the feces contained approximately two times as much radioactivity as the urine, and 50 to 70 percent of the total activity was excreted during the collection period. As mentioned in the Metabolism section of this report, the proportion of metabolites varied between the mouse and the rat.

Although there has been extensive work done on the metabolism and excretion of dieldrin in animals, there is understandably less known about the fate of dieldrin in humans. Early work by Cueto and Hayes (1962) demonstrated that dieldrin and some of its metabolites could be detected in the urine of occupationally exposed workers. A later report by Cueto and Biros (1967) compared the levels of dieldrin and other chlorinated insecticides in the urine of 5 men and 5 women in the general population to that of 14 men with different degrees of occupational exposure. The concentrations of dieldrin found in the urine of men and women in the general population were 0.8 ± 0.2 mg/l, and 1.3 ± 0.1 mg/l, respectively. The concentrations found in male workers with low, medium, and high degrees of exposure were 5.3 mg/l (5), 13.8 mg/l (4), and 51.4 mg/l (5), respectively (numbers in parentheses represent the number of individuals per sample). The degrees of exposure were only expressed as relative and no data on the exposures were given.

Hayes and Curley (1968) measured the plasma, fat, and urine concentration of various chlorinated pesticides in workers with occupational exposure to these chemicals. In 14 urine samples, aldrin was present at less than 0.2 mg/l and dieldrin was present at 1.3 to 66.0 mg/l. This is compared to the mean for dieldrin in the general population of 0.8 ± 0.2 mg/l determined in the same laboratory by Cueto and Biros (1967).

A study by Hunter, et al. (1969) concluded that dieldrin had a relatively long half-life in humans. This compares with a half-life of less than ten days reported in animal studies. In the Hunter, et al. study, 12 human volunteers ingested various doses of dieldrin for up to 24 months. The blood and adipose concentrations were determined over this time and the blood levels were followed for eight additional months after termination of the treatment. The authors reported that during this period concentrations of dieldrin in the blood of three of the volunteers did not change significantly. (These concentrations were not given). In the other nine subjects, the half-life of dieldrin in the blood ranged from 141 to 592 days with a mean of 369 days. These estimates were made on a limited number of samples.

Jager (1970) reported that DeJonge, in an unpublished report, studied the half-life of dieldrin in the blood of 15 aldrin/dieldrin workers who were transferred to other areas. Prior to transfer, these workers had had high exposures to the pesticides and concentrations of aldrin/dieldrin in their blood had reached equilibrium. Measurements of the dieldrin blood concentrations were taken every six months for three years following the transfer. The mean half-life was 0.73 years (approx. 266 days). This is somewhat in agreement with the estimates of Hunter, et al. (1969) of 369 days based on limited data.

It has been reported by these and other authors (Robinson, et al. 1969; Walker, et al. 1969) that there is a direct relationship between the concentration of dieldrin in the blood and that in adipose and other tissues. It seems likely that the half-life in the blood may reflect the overall half-life in other tissues.

EFFECTS

Acute, Subacute, and Chronic Toxicity

The acute toxicity of aldrin and dieldrin has been extensively summarized by Hodge, et al. (1967) and Jager (1970). In many cases, aldrin and dieldrin are considered similar due to the rapid conversion of aldrin to dieldrin (see Metabolism section). Dieldrin, in turn, is metabolized to a variety of more polar products. In some cases, the toxicity of the metabolites has been compared to the parent compound but this information is rather sparse (Soto and Deichmann, 1967).

After ingestion, aldrin and dieldrin are rapidly absorbed from the gastro-intestinal tract. Following absorption, the pesticides are transported from the liver to different sites in the body. They have been found at various levels in the brain, blood (including erythrocytes), liver, and especially the adipose tissue (Mick, et al. 1971; Walker, et al. 1969). In addition, dieldrin has been shown to cross the placenta to the fetus (Hathaway, et al. 1967). Hunter, et al. (1969) demonstrated that a relationship between intake and storage exists and that a plateau is maintained in the tissues unless the dose changes considerably.

It was shown early that the pesticide-to-solvent ratio affects the LD_{50} (Barnes and Heath, 1964) and that some variation is caused by the solvent employed (Heath and Vandekar, 1964). There is a pronounced variation in toxicity related to route of administration. Toxicity is highest by the intravenous route, followed by oral, then dermal. This is most likely due to the high blood and central nervous system concentrations produced from intravenous injection. Oral and dermal toxicity is lower due to lower blood concentrations brought about by resorption and storage in adipose tissue. For most species the acute oral toxic dose is between 20 and 70 mg/kg. This includes the rat, mouse, dog, monkey, sheep, and man (Hodge, et al. 1967).

With both aldrin and dieldrin, toxicity in animals appears to be related to the central nervous system. According to Hodge:

> ...a characteristic pattern has been described of stimulation, hyperexcitability, hyperactivity, incoordination, and exaggerated body movement, ultimately leading to convulsion, depression, and death.

There apparently is a direct correlation between blood concentrations and clinical signs of intoxication. Keane, et al. (1969) reported that in dogs fed daily doses of dieldrin, the first signs of muscle spasms occurred at 0.38 to 0.50 µg/ml blood and convulsions at 0.74 to 0.84 µg/ml.

The symptoms of intoxication in man are similar to those found in mice, rats, and dogs. Jager (1970) described the symptoms resulting from oral or dermal exposure that occur from 20 minutes to 24 hours as:

> ...headache, dizziness, nausea, general malaise, vomiting, followed later by muscle twitching, myoclonic jerks and even convulsions. Death may result from anoxemia.

Changes in the electroencephalogram (EEG) usually result after insecticide intoxication and generally return to normal after discontinuance of exposure (Hoogendam, et al. 1962). The transitory change in the EEG has been challanged by several investigators (see Burchfiel, et al. (1976) for recent summary). Work carried out in Rhesus monkeys (Burchfiel, et al. 1976) using technical grade dieldrin (4 mg/kg, i.v. one time or 1 mg/kg i.m. administered once a week for 10 weeks) demonstrated that dieldrin can alter the EEG for up to 1 year.

The acute lethal dose of aldrin in man was reported by Jager (1970) and Hayes (1971) based on the summary of Hodge, et al. (1967) to be 5 g or 70 mg/kg, respectively. However, Hodge, et al. only speculated on possible human toxic effects from a 1-year feeding study in monkeys. It is known that persons have recovered from acute oral doses of 26 mg/kg aldrin and 44 mg/kg dieldrin so that the acute lethal human dose might be somewhat higher (Hayes, 1971).

The subacute or chronic toxicity of low doses of aldrin and dieldrin to mice, rats, dogs and, to some extent, monkeys, has been reported in many of the carcinogenicity studies included herein. The resulting effects include shortened life span, increased liver-to-body weight ratio, various changes in liver histology, and induction of hepatic enzymes. Another effect that has been observed is teratogenicity (Ottolenghi, et al. 1974).

Some information is available concerning the subacute or chronic exposure of humans to aldrin and dieldrin. Based on information gained from monitoring workers at the Shell Chemical Company, Jager (1970) reported that 33.2 µg/kg/day can be tolerated by workers for up to 15 years. Above this level some individuals may show signs of intoxication, although others can tolerate two times this level. In another study involving 12 volunteers who ingested dieldrin for up to two years, 3.1 µg/kg/day was tolerated and produced no increase in plasma alkaline phosphatase activity (Hunter, et al. 1969).

Synergism and/or Antagonism

Since aldrin and dieldrin are metabolized by way of the mixed function oxidases (MFO), it must be assumed that any inducer or inhibitor of these enzymes will affect the metabolism of aldrin or dieldrin. Dieldrin and other organochlorine pesticides have been reported to induce the MFO (Kohli, et al. 1977). Baldwin, et al. (1972) reported that prefeeding low doses of dieldrin to rats altered the metabolic products produced after acute dosing. Several reports have appeared on the combined effect of aldrin or dieldrin on the storage of DDT in tissues (Street, 1964; Street and Blau, 1966; Deichmann, et al. 1969).

In the Deichmann, et al. (1969) study when aldrin was given along with DDT or after a plateau had been reached in the blood and fat by chronic DDT feeding. The retention of DDT by the blood and fat increased considerably in the animals given both chemicals as compared to the animals only given DDT. The authors suggest that this increase in tissue DDT concentrations is due to a reduced rate of excretion of DDT.

Walker, et al. (1972) fed groups of mice 50 or 100 mg/kg/diet DDT or a mixture of 5 mg/kg/diet dieldrin and 50 mg/kg/diet DDT for 112 weeks. The highest incidence of tumors was in the dieldrin/DDT group, although it is difficult to determine whether the effect between dieldrin and DDT was additive or synergistic.

Clark and Krieger (1976) studied the metabolism and tissue accumulation of ^{14}C-labeled aldrin (99.3 percent purity) in combination with an inhibitor of oxidative biotransformation (i.e., SKF 525-A). They reported that pretreatment of male Swiss-Webster mice with either 50 or 100 mg/kg SKF 525-A significantly increased the accumulation of radioactivity in the blood, brain, kidney, and liver. The SKF 525-A blocked the epoxidation of aldrin to dieldrin. However, the authors did not feel that differences in metabolite formation or excretion alone could account for the increased accumulation in the tissues.

Teratogenicity

In 1967, Hathaway, et al. established that ^{14}C-dieldrin could cross the placenta in rabbits. Eliason and Posner (1971a,b) demonstrated that ^{14}C-dieldrin crossed the placenta in the rat and that the concentration in the maternal plasma increased as gestation progressed. Deichmann (1972) reported that 25 mg/kg/diet aldrin and dieldrin fed to mice for six generations markedly affected such parameters as fertility, gestation, viability, lactation, and survival of the young, while mice fed lower doses showed fewer or no effects.

In a study by Ottolenghi, et al. (1974) pregnant golden hamsters and pregnant CD-1 mice were given single oral doses of purified aldrin, dieldrin, or endrin at one-half the LD_{50} (hamsters 50, 30, 5 mg/kg, and mice 25, 15, 2.5 mg/kg, respectively). The hamsters were treated orally on day seven, eight, or nine of gestation and the mice on day nine. All three pesticides caused a significant increase in fetal death in hamsters treated on days seven and eight. Only dieldrin gave significant results on day nine. Hamsters treated on day eight also had the highest number of anomalies (i.e., open eye, webbed foot, cleft palate, and others). These increased anomalies were noted for all three pesticides. The three pesticides also reduced the fetal weight in the hamsters treated on the three different days. No significant difference was observed in the weight or survival of fetuses of treated and control mice; however, a teratogenic effect was observed in mice for all three pesticides. It was less pronounced in the mice than in the hamsters. The author reasoned that the reduced teratogenic effect in mice may be due to the lower doses used in the mice.

Two later studies on the teratogenicity of dieldrin have reached different conclusions. The studies of Chernoff, et al. (1975) and Dix, et al. (1977) both concluded that dieldrin was not teratogenic. Chernoff, et al. tested dieldrin (87 percent purity) and the photo-product, photodieldrin (95 percent purity) in CD-1 mice and CD rats orally at doses lower than those used by Ottolenghi, et al. (1974). The actual doses of dieldrin based on 87 percent purity were 1.3, 2.6, and 5.2 mg/kg/day over a ten-day period (i.e., days 7 to 16 of gestation). The compounds were dissolved in peanut oil. The control animals also received peanut oil. The highest doses of dieldrin produced 41 percent mortality in rats. In mice the highest doses induced significant increases in liver-to-body weight ratios, reduced the weight gain, and produced some fetal toxicity. Photodieldrin at 0.6 mg/kg/day for 10 days also induced a significant increase in the liver-to-body weight ratio in rats but caused no fetal toxicity. However, no teratogenic effects were observed in the mice or rats at any of the doses employed.

Dix, et al. (1977) examined the use of two solvents (corn oil and dimethylsulfoxide (DMSO)) with various doses of dieldrin in CF1 mice. The corn oil groups received 1.5 or 4.0 mg/kg/day of 99 percent pure dieldrin orally with suitable controls of corn oil or no treatment. The DMSO groups received 0.25, 0.5, or 1.0 mg/kg/day with similar controls. Both solvent groups were treated on days 6 through 14 of gestation. In the corn oil group, young (7-week) virgin animals were used and the pregnancy rate was very low. With the few animals that survived to term, the only significant effect was delayed ossification in fetuses of the mice administered the 4 mg level. The DMSO experiments were conducted with older animals (ten weeks) of proven fertility. Fetuses of these animals demonstrated a significant increase in incidences of delayed ossification and extra ribs. However, the DMSO controls also had a high incidence of these two anomalies. The authors attributed this to the toxic effect of this solvent. DMSO also produced a reduction in maternal and fetal body weights whereas the corn oil did not. No differences were observed in the mean litter size, number of resorptions, or fetal death with either solvent.

Mutagenicity

Relatively little work has been done on the mutagenicity of aldrin or dieldrin. Of the limited data available, most are concerned with the mutagenicity of dieldrin. This may be sufficient, since aldrin is readily converted to dieldrin in both *in vivo* and *in vitro* systems. Fahrig (1973) summarized the microbial studies carried out up to 1973 on aldrin, dieldrin, and other organochlorine pesticides including DDT and the metabolites of DDT. Aldrin and dieldrin gave negative results with gene conversion in Saccharomyces cerevisae, back-mutation in Serratia marcescens, forward mutation (Gal R^S) in Eschericia coli and forward mutation to streptomycin resistance in E. coli. It is important to note that DDT and several of its metabolites also gave negative results in these microbial tests and that no mention of any type of activation system (i.e., mammalian liver enzymes) was made in this summary.

Bidwell, et al. (1975) reported in an abstract that dieldrin was not found to be mutagenic in five strains of Salmonella typhimurium with or without the addition of a liver activation system, although the authors did not give dose levels. They also stated that dieldrin was negative in the host-mediated assay, blood and urine analysis, micronucleus test, metaphase analysis, dominant lethal test, and heritable translocation test. The doses used were 0.08, 0.8, and 8.0 mg/kg in corn oil with corn oil used as the control and triethylene melamine (0.5 mg/kg five times) serving as the positive mutagenic control. The pesticide was given orally on a subacute basis.

Dean, et al. (1975) evaluated dieldrin (99+ percent purity) in two dominant lethal assays in CF1 mice, for chromosomal damage in male and female Chinese hamsters and in the host-mediated assay with Saccharomyces cerevisiae in CF1 male mice.

Two dominant lethal assays were carried out, one with a single oral dose of 12.5 or 25 mg/kg and the other with a single oral dose of 12.5, 25 or 50 mg/kg. The treatment groups consisted of 8 males and the DMSO solvent control groups of 16 males. In both experiments, each male was caged with three females for 7 days. This was repeated for 8 weeks in the first study and for 5 weeks in the second. Also, in the first experiment 8 mice received cyclophosphamide at 100 mg/kg orally as a positive control. In all cases, dieldrin was dissolved in DMSO and the control animals were given DMSO. The females were killed and examined 13 days after the mid-week of being caged with the males. All of the dieldrin-treated males demonstrated signs of intoxication. One of the cyclophosphamide-treated males died 7 days after treatment. Neither dieldrin nor cyclophosphamide produced significant changes in the pregnancy rate of the female mice. However, when overall means of the total fetal implants per pregnancy were examined, the 12.5 mg/kg and the cyclophosphamide-treated groups were significantly lower than the controls (P 0.05 and P 0.001, respectively) in the first experiment. Conversely, the overall means for the 25 mg/kg group in the second experiment was significantly higher than the control group (P 0.05).

In the cytogenetic studies using Chinese hamsters, four males and four females were administered either DMSO, or dieldrin dissolved in DMSO at 30 or 60 mg/kg orally. Two animals of each sex were killed at 8 and 24 hours after treatment and slides were prepared from the femurs. One hundred cells were analyzed from the bone marrow of each animal. While there is some problem determining the actual number of animals employed and the number of cells examined[2], there appears to be no significant differences in gaps or polyploidy between treated or control hamsters. It should be

[2] The authors state in the results that 4,800 cells were analyzed from 48 animals. However, from the methods section it appears that only 24 animals were used in this study.

noted that it appears that only two males and two females were examined at each time/dose point and this is a very small sample size when trying to determine small increases as the authors are doing.

Another part of this study looked at mitotic gene conversion in Saccharomyces cerevisiae D4 at the ade_2 and trp_5 loci in a host-mediated assay using male, CF1 mice. The experiments were divided into three single dose and three multiple dose (5) protocols. In the single dose treatments, mice received either DMSO, or dieldrin dissolved in DMSO, orally at 25 or 50 mg/kg orally. The multiple treatments consisted of DMSO or 5 or 10 mg/kg dieldrin orally for 5 days. There were two mice per treatment group and the yeast were injected i.p. either immediately after the single treatment or the final multiple treatment. Ethyl methane-sulfonate (EMS) was given orally at 400 mg/kg as a single dose. A small proportion of the animals receiving dieldrin at 10 mg/kg for 5 days did not survive but this is not reflected in the results given. The table summarizing the results of the host-mediated assay states that two mice per group were used but the number for the three experiments is obviously less than six if all the mice did not survive. Of those that did survive, only the EMS treatment groups had significant increases in adenine and tryptophan convertants.

Three reports on the mutagenicity of aldrin or dieldrin have recently been published. The first examined the mutagenicity of dieldrin and several other pesticides with four strains of S. typhimurium (i.e., TA1535, TA1536, TA1537, and TA1538) with the addition of a rat liver activating system (Marshall, et al. 1976). The second, an in-depth study of nearly 200 pesticides, utilized several microbial indicators and, in some cases, the addition of an activating system (Shirasu, et al. 1977). The third study dealt primarily with strains of S. typhimurium (TA1535, TA100, and TA98) plus a mouse liver activating system (Majumdar, et al. 1977).

In the Marshall, et al. (1976) study, dieldrin was tested at only one concentration, 1,000 µg per plate, with and without the addition of phenobarbital induced rat liver homogenate. In all four strains tested, no increase in mutagenicity was observed at this concentration.

Shirasu, et al. (1977) assayed aldrin with metabolic activation using E. coli B/r WP2 try-hcr$^+$ and WP try-hcr$^-$ and S. typhimurium strains TA1535, TA1537, TA98, and TA100. Dieldrin was assayed without metabolic activation using the E. coli WP2 hcr$^+$, WP2 hcr$^-$ and S. typhimurium TA1535, TA1536, TA1537, and TA1538. According to the authors, both aldrin and dieldrin were considered nonmutagenic in these tests.

Wade, et al. (1979) have evaluated dieldrin using S. typhimurium strain TA100 and TA98 both with and without a rat liver activating system. Their assay was in the form of a spot test at 50 and 1,000 µg per plate. At these two levels, dieldrin failed to produce any mutagenic response.

Majumdar, et al. (1977), on the other hand, have reported that dieldrin was somewhat mutagenic for S. typhimurium strains TA1535, TA100, and TA98 without metabolic activation and that it was strongly mutagenic for all three strains when liver enzymes from Aroclor-1254[3]-induced mice were added to the mixtures.

---

[3] Aroclor-1254 is a mixture of PCBs, which induce the MFO in liver (Ames, et al. 1975).

In summarizing the limited microbial mutagenicity studies on aldrin and dieldrin, it must be mentioned that the only reference to any mutagenicity in the Majumdar studies contains several notable inconsistencies. The inconsistencies are: (1) the cultures used were grown for 24 hours rather than the recommended 16 hours; (2) the plates were incubated for 72 hours rather than the conventional 48 hours; and (3) the control values for TA1535 and TA98 were not consistent with those recommended by Ames, et al. (1975).

It is not possible to say that these inconsistencies could account for the positive mutagenic findings but they should be taken into consideration in view of the fact that several other similar, although not identical, studies reported no mutagenic findings with dieldrin. It should be kept in mind that mice apparently metabolize dieldrin differently than do rats (see the Metabolism section of this report). It is possible that the use of the mouse liver enzymes by Majumdar, et al. (1977) may be producing a mutagenic metabolite not seen in other studies.

Studies on the mutagenic effects of dieldrin in organisms other than microorganisms were also somewhat varied. Scholes (1955) reported that dieldrin had no effect on onion root mitosis. However, Markaryan (1966) observed an increase in the cytogenic effects of dieldrin in mouse bone marrow nuclei and Bunch and Low (1973) reported chromosomal aberrations in semi-domestic mallard ducks.

Recently, Majumdar, et al. (1976) studied (1) the effect of dieldrin on chromosomes in mouse bone marrow *in vivo* and in cultured human WI-38 lung cells, and (2) the cytopathic effect of dieldrin on the cultured human WI-38 cells. They reported a decrease in the mitotic index in both the *in vivo* mouse bone marrow and *in vitro* human lung cells with the increasing concentration of dieldrin used. In each test, an increase in chromosome aberrations was observed with the lowest doses employed (1 mg/kg in mouse bone marrow and 1 µg/ml in human cell cultures). The authors also reported a dose- and time-dependent cytotoxic effect on the WI-38 human lung cells.

In addition, Ahmed, et al. (1977a) measured unscheduled DNA synthesis (UDS) in SV-40 transformed VA-4 human fibroblasts *in vitro* with and without an uninduced rat liver activating system using aldrin, dieldrin, DDT, and other pesticides. Both aldrin and dieldrin produced a significant increase in UDS either with or without the activating system at all the doses used.

Another study by this group (Ahmed, et al. 1977b) demonstrated that dieldrin induced ouabain resistance in Chinese hamsters V79 cells when tested at a concentration of 0.01 M. With a cell survival of 77.8 percent, they obtained a mutation frequency of 16.4 mutants per 10^6 survivors as compared to 1.8 per 10^6 for the controls.

Carcinogenicity

During the 1960's and the early part of the 1970's, numerous studies on the carcinogenicity of aldrin and dieldrin appeared in literature. These reports include studies on mice, rats, dogs, and monkeys. Of these species, mice appear to be the most susceptible to aldrin/dieldrin. Various strains of both sexes have been examined at different dose levels. The effects range from benign liver tumors to hepatocarcinomas with transplantation confirmation to pulmonary metastases. The data on carcinogenicity have been evaluated and discussed extensively, mainly by Epstein (1975a,b, 1976).

Six major studies using various strains of mice have been carried out mainly by long-term feeding at low doses (i.e., 0.1 to 20 mg/kg in the diet). The earliest of these studies was conducted by the U.S. Food and Drug Administration (FDA) (Davis and Fitzhugh, 1962). Using C_3HeB/Fe (C_3H) mice, both males and females were fed either aldrin or dieldrin at 10 mg/kg in the diet for two years. Both aldrin and dieldrin shortened the average life span by two months. The experimental and control group death rate was high, possibly due to overcrowding. Significantly more hepatomas were observed in the treated groups than in the controls for both sexes. In addition, the number of mice with tumors may have been underestimated due to the high mortality which left fewer animals for evaluation.

In an FDA follow-up study, Davis (1965) examined 100 males and females of the C_3H mice treated with aldrin or dieldrin at the same concentrations as the first study. Again, survival was reduced compared to the control group and there was an increase in benign hyperplasia and benign hepatomas. A re-evaluation of the histological material of both of these studies was carried out by Rueber in 1973 (Epstein, 1975a,b, 1976). He concluded that the hepatomas were malignant and that both aldrin and dieldrin were hepatocarcinogenic for male and female C_3H mice.

In a 1964 abstract, Song and Harville reported some indication of hepatocarcinogenicity in C_3H and CBA mice with aldrin (15 mg/kg) and dieldrin (15 mg/kg) although minimal data are given. Epstein (1975a,b, 1976) reviewed an unpublished study of MacDonald, et al. on technical grade dieldrin in Swiss-Webster mice. The authors concluded that dieldrin was noncarcinogenic but that there was some questions as to the type of lesions.

Walker, et al. (1972) conducted a multi-part study of dieldrin in CF1 mice of both sexes. In this study, the dieldrin used was 99+ percent pure and 4-amino-2,3-dimethylazobenzene (ADAB) was used as the positive control. In the first part of the study, diets were prepared containing 0, 0.1, 1.0, and 10 mg/kg dieldrin although 0.01 mg/kg dieldrin was found in the control (0 mg/kg) diet along with low concentrations of other pesticides. The treatment groups were made up of 600, 250, 250, and 400 mice, respectively, and contained equal numbers of males and females. The ADAB group, which contained 50 mice equally divided as to sex, received 600 mg/kg/diet for six months. Initially, the animals were housed five to a cage, but after the sixth week they were placed in individual cages. The positive controls were maintained separately from the other groups. After nine months, the mice receiving 10 mg/kg in the diet dieldrin demonstrated palpable intra-abdominal masses, and by the fifteenth month, half the males and females in the group had died or had been killed when the masses became large. This period of 15 months is short compared to the 20 to 24 months that elapsed before one-half of the control group had died. The life spans of members of the 0.1 mg/kg and 1.0 mg/kg groups were similar to those of the controls. All the ADAB mice were dead by the 15th month.

An increased number of liver tumors was observed at all the concentrations of dieldrin including 0.1 mg/kg, with the highest increase occurring in the 10 mg/kg group. The tumors were classified by the authors as type (a) "...solid cords of closely packed parenchymal cells with a morphology and staining affinity little different from the rest of the parenchyma," or (b) "...areas of cells proliferating in confluent sheets and often with foci of necrosis. These lesions were distinguished from the previous types of growth by the presence of areas of papilliform and adenoid formations of liver cells with wide and irregular vascular channels within the growth." This classification appears somewhat arbitrary. Nonetheless, the presence of tumors was dose-related and effects were detected at the lowest dieldrin level tested (0.1 mg/kg). In addition to the increase in hepatic tumors there was an increase in the incidence of tumors at other sites.

In the second part of the Walker, et al. (1972) study, groups of 30 male and 30 female CF1 mice received ethylene oxide-sterilized diets containing 1.25, 2.5, 5, 10, or 20 mg/kg dieldrin for 128 weeks. The control group consisted of 78 males and 78 females and the conditions and observations were similar to those in the first experiment. In this part of the study, the mice that received 20 mg/kg dieldrin in the diet had a high mortality rate. About 25 percent of the males and 50 percent of the females showed signs of intoxication and died during the first 3 months. Liver masses were detected at 36 weeks, and all the mice either died or were killed at 12 months. Masses were not detected until 40 weeks in the 10 mg/kg mice, 75 weeks in the 5 mg/kg mice, and 100 weeks in the 2.5 mg/kg mice. In the 10 and 20 mg/kg groups, few animals were available for examination due to the acute toxicity or their being used in another study. The 5 mg/kg group had a higher incidence of tumors than the 2.5 mg/kg group.

The third part of the study was carried out under similar conditions. Groups of 60 mice received gamma-irradiated diets containing 0 or 10 mg/kg/diet dieldrin for 120 weeks. Also, groups of 48 mice received gamma-irradiated diets and litter for 110 weeks or unsterilized diets and litter for 104 weeks. The authors stated that liver enlargement occurrence and mortality were similar to those of the previous study.

The next section of the Walker, et al. (1972) study concerned the combined effect of dieldrin and DDT treatment on CF1 mice. Initially, the mice were fed diets containing 200 mg/kg DDT or 10:200 mg/kg dieldrin:DDT. This resulted in high mortality. The diets were subsequently reduced to 50 and 100 mg/kg DDT and 5:50 mg/kg dieldrin:DDT. There were 47 males and 47 females in the control group and 32 males and 32 females in each of the treatment groups. In mice on the 5:50 mg/kg diet and 100 mg/kg DDT diet, liver enlargements were detected after 65 weeks of exposure. Both of these doses were toxic to males but only the 5:50 mg/kg dose was toxic to females. At 50 mg/kg DDT, masses were detected by the 96th week but the mortality was similar to that of the controls. In this experiment, the highest incidence of liver tumors was in the dieldrin:DDT group. However, because only one combination was tested, it is difficult to determine whether the effect was synergistic or additive. In a re-evaluation of the experiment, Reuber (see Epstein, 1975a,b, 1976), believes that Walker, et al. (1972) over-estimated the incidence of liver tumors in the control and DDT groups, thus minimizing the effect of the combined dieldrin/DDT.

In the last section of the Walker, et al. (1972) study, groups of 58 mice were fed dieldrin at 10 mg/kg for 2, 4, 8, 16, 32, and 64 weeks and sacrificed after 2 years. The control group consisted of 156 mice. All groups were equally divided between males and females. In the mice receiving dieldrin for 64 weeks, liver enlargements were detected after 60 weeks in six males and two females. These enlargements remained after the termination of the feeding. No other enlargements were detected and the mortality of all the groups was similar throughout the 2 years. It is important to note that type b tumors were detected after only 4 or 8 weeks of treatment and that the liver enlargements did not appear after the feeding was terminated.

A similar study of dieldrin and other chemicals in CFl mice was carried out by the same group (Thorpe and Walker, 1973). The treatment groups were comprised of 30 males and 30 females and the controls of 45 mice of each sex. Dieldrin was tested at one concentration (10 mg/kg/diet) only, and the animals were not sacrificed when abdominal masses were large as in the previous studies. The study was terminated after 100 weeks of feeding. The authors reported that there were no signs of intoxication in the dieldrin groups; however, mortality increased after 22 months of exposure.

Also liver enlargements were detected in both sexes by the 50th week. In this study, the cumulative tumor incidence and the number of dead mice were given at 17, 21, 25, and 26 months. Dieldrin at 10 mg/kg produced a high incidence of liver tumors. All the males and one-half the females that had died by 17 months had liver tumors. By the end of the study, 100 percent of the males and 87 percent of the females had liver tumors.

In a recent evaluation of both aldrin and dieldrin by the National Cancer Institute, aldrin and dieldrin were found to produce hepatic carcinomas in male mice. Female mice responded to low doses of dieldrin, but showed no effects from aldrin. No carcinomas were observed in either male or female rats of two different species (43 FR 2450) when the subjects were exposed to both aldrin and dieldrin. In the study on mice, groups of 50 male and 50 female B6C3F1 mice were fed either aldrin (technical grade) or dieldrin (technical grade) at various doses. The females received aldrin at 3 and 6 mg/kg/diet and the males received aldrin at 4 and 8 mg/kg. Both sexes were given dieldrin at 2.5 and 5 mg/g. Aldrin controls consisted of 20 untreated males and 10 females and dieldrin controls had 20 animals per group. In addition, pooled controls consisted of 92 males and 78 females. The animals were fed the pesticide diets for 80 weeks and then observed for 10 to 13 weeks. All survivors were killed at 90 to 93 weeks.

In the male mice administered aldrin, there was a significant, dose-related increase in the incidence of hepatic carcinomas. The values were: matched controls 3/20 (15 percent); pooled controls 17/92 (19 percent); 4 mg/kg 16/49 (33 percent); and 8 mg/kg 25/45

(56 percent). The mean body weights of the aldrin- and dieldrin-fed mice were similar in the control and treated groups. There was a dose-related mortality in female mice at the high dose of aldrin. With the male mice fed dieldrin, a significant increase in hepatic-carcinomas was observed in the 5 mg/kg group. The incidences were 12/50 (24 percent) for the 2.5 mg/kg group and 16/45 (36 percent) for the 5 mg/kg group.

There have also been six carcinogenicity studies of aldrin and/or dieldrin done in various strains of rats. In an early paper by Treon and Cleveland (1955) aldrin and dieldrin were fed to male and female Carworth rats at 2.5, 12.5, and 25 mg/kg. The authors reported a significant increase in mortality and an increase in liver-to-body weight ratios at all concentrations tested. No data on tumor incidences were given, although some liver lesions were detected. Later Cleveland (1966) summarized the work on aldrin and dieldrin conducted at the Kettering Laboratory. Although little data and details were given, Cleveland stated that aldrin and dieldrin were not tumorigenic in their rat studies.

A study was carried out by the U.S. Food and Drug Administration on aldrin and dieldrin in rats and dogs (Fitzhugh, et al. 1964) to determine the toxicity of these pesticides. Groups of 12 male and 12 female Osborne-Mendel rats were fed diets containing either aldrin (99+ percent purity) or dieldrin (100 percent purity) at 0, 0.5, 2, 10, 50, 100, or 150 mg/kg for two years. The animals were housed individually and the survivors were killed after two years. None of the dose levels of aldrin or dieldrin affected the growth of the rats but both chemicals at 50 mg/kg or greater reduced the survival. A significant increase in liver-to-body weight ratios was observed in both males and females for several doses of both chemicals. The authors reported no increase in liver tumors; however, there was a high incidence of multiple site tumors at lower concentrations of both aldrin and dieldrin.

Deichmann, et al. (1967) carried out a study in which 5 mg/kg aldrin (technical grade) was fed to male and female Osborne-Mendel rats, either individually or in combination with 200 mg/kg aramite, 200 mg/kg DDT, and 1,000 mg/kg methoxychlor. There were 30 males and 30 females in each treatment group and they were housed in pairs. No increase in mortality over the controls was observed in any of the treated groups. Aldrin alone had no significant effect on liver-to-body weight ratio, but an increase in the ratio was noted in the groups treated with the pesticide mixtures. The authors state that one-half (13 females and 2 males) of the aldrin-treated rats had one tumor; however, only the tumors in survivors were listed.

Walker, et al. (1969) fed dieldrin (99+ percent purity) to Carworth rats at concentrations of 0, 0.1, 1.0, and 10 mg/kg in the diet for two years. There were 25 males and 25 females in each treatment group and 45 rats of each sex in the control group. The animals were housed individually and dying animals were killed and examined. The authors reported that some irritability, tremors, and convulsions occurred after two to three months but that the animals remained in good health for the two years. None of the dieldrin doses had any effect on body weight. Mortality was the same for the control and treated groups; however, all the groups had an overall, high rate of mortality. This resulted in only a few animals being available for examination at the conclusion of the feeding. At 1 and 10 mg/kg there were increases in liver-to-body weight ratios. Only one male rat and four female rats at the 10 mg/kg level demonstrated any liver cell changes. However, at the 0.1 and 1.0 mg/kg levels there were high but not significant increases in total tumors even though few animals were examined histologically.

In another study with the Osborne-Mendel rat, Deichmann, et al. (1970) examined aldrin, dieldrin, and endrin in a lifetime exposure. Aldrin (technical, 95 percent) and dieldrin (technical[4], 100 percent active ingredients) were fed in the diet to groups of 50 males and 50 females. The concentrations during the first two weeks were 10, 15, and 25 mg/kg aldrin and 10, 15, and 25 mg/kg dieldrin. After this time all the dose concentrations were doubled for the remainder of the treatment time. The control groups contained 100 rats of each sex. Any animals that appeared ill were sacrificed. Both aldrin and dieldrin produced some dose-related toxicity, tremors, and clonic convulsions, especially in females. However, these doses had no effect on mean gain in body weight although some animals had marked loss of weight. The mean survival rate was somewhat lower in the aldrin and dieldrin rats; again, predominantly in females receiving the high concentrations. There were significant increases in liver-to-body weight ratios in males fed aldrin at 30 and 50 mg/kg and dieldrin at 30 mg/kg and a significant decrease in liver-to-body weight ratios in females fed aldrin at 20 mg/kg. A moderate increase in hepatic centrilobular cloudy swelling and necrosis was observed in both male and female rats fed aldrin and dieldrin as compared to the controls. However, there was no increase in the number of liver tumors or other site tumors. In fact, a decrease in total tumors was observed in both the males and females fed aldrin and dieldrin. The authors stated that this was possibly due to increased microsomal enzyme activity. It should be noted that limited re-evaluation of this data was carried out by Reuber who disagreed with the findings of Deichmann, et al. (1970). However, he re-evaluated only one group (dieldrin, 30 mg/kg) and there has been no independent re-evaluation of the material.

---

[4] This is somewhat contradictory since "technical" dieldrin is actually 85 percent pure.

A two-year study by the National Cancer Institute (1976)(43 FR 2450) studied the effects of technical grade aldrin and dieldrin on Osborne-Mendel and Fisher 344 rats. The first part of the study used groups of 50 Osborne-Mendel rats of each sex for aldrin (30 or 60 mg/kg) and dieldrin (29 or 65 mg/kg). Aldrin was fed to the males for 74 weeks. The rats were then observed for an additional 37 to 38 weeks. All survivors were killed at 111 to 113 weeks. The same doses of aldrin were administered to the female rats for 80 weeks, followed by 32 to 33 weeks of observation. All survivors were killed at 111 to 113 weeks. The dieldrin rats were treated for 59 weeks at 65 mg/kg followed by 51 to 52 weeks of observation, or 80 weeks at 29 mg/kg followed by 30 to 31 weeks of observation. All survivors were killed at 110 to 111 weeks. For both pesticides, the controls consisted of 10 untreated rats of each sex plus pooled controls consisting the matched control groups combined with 58 untreated males and 60 untreated females from similar bioassays of other chemicals.

During the first year of the rat studies, the mean body weights for the aldrin- and dieldrin-fed rats did not differ from those of the controls. However, during the second year, the body weights of the treated rats were lower than those of the untreated. For both aldrin and dieldrin, no significant increase in hepatic carcinomas was observed in either sex. There was a significant increase in adrenal cortical adenoma in the low-dose aldrin- and dieldrin-treated female rats.

In the second part of the study on rats, 24 male and 24 female Fisher 344 rats were fed purified dieldrin at 2, 10, or 50 mg/kg of diet for 104 to 105 weeks. Matched controls consisted of 24 rats of each sex. All survivors were killed at 104 to 105 weeks. The body weights of the treated and control rats were similar and survival was not greatly affected. The high-dose males and females demonstrated signs of intoxification at 76 and 80 weeks, respectively. A variety of neoplasms occurred in both the control and treated rats; however, there were no significant dose-related increases in the neoplasms.

To date, there has been only one carcinogenicity study reported on either aldrin or dieldrin in hamsters. Cabral, et al. (1979) carried out lifetime feeding studies in Syrian golden hamsters with dieldrin (99 percent purity). Groups of nearly equal size (i.e., 32-41 per group) of male and female hamsters were fed a diet containing 0, 20, 60 or 80 mg/kg for up to 120 weeks at which time the remaining survivors were killed. While there was no decrease in survival at 50 weeks, the numbers of females remaining at 70 weeks was one-half or less than the males. At 90 weeks the survival rate was about 10 percent for all groups except the males of the 180 mg/kg level which had 32 percent survivors. Both males and females at the low and high doses demonstrated a marked retardation of growth. The authors state that there was no significant difference between the percentage of control animals with tumors and the treated animals with tumors. However, in the treated groups, more animals had more than one tumor than in the control groups. Although there was an increase in the number of animals with adrenal tumors, especially males, again this was not statistically significant. In the animals receiving the high dose of dieldrin, there was one male and one female which had hepatomas. It was also noted by these authors that there was a dose-related increase in the incidence of hepatic cell hypertrophy in the dieldrin-treated hamsters.

There has been minimal work on the carcinogenicity of aldrin or dieldrin in dogs. A limited, short-term study was conducted by Treon and Cleveland (1955). Aldrin and dieldrin were fed to two male and two female beagles at 1 and 3 mg/kg/diet. The dogs were killed between 15 and 16 months. Although the growth rates of the treated dogs were similar to those of the controls, liver weights were increased at 1 mg/kg. These doses were toxic to the dogs and mortality was high. The study provides few data on the necropsy and the treatment was too short to adequately evaluate carcinogenicity.

In another study using dogs, Fitzhugh, et al. (1964) treated 26 animals with aldrin or dieldrin at dosages of 0.2 to 1.0 mg/kg/day, 6 days a week, up to 25 months. At doses of 0.5 mg/kg and greater, toxic effects including weight loss, convulsions, and death were observed. At 1 mg/kg/day or higher no animals survived over 49 days, and at 2.5 and 10 mg/kg/day all dogs died within 10 weeks. However, dogs fed 0.2 mg/kg/day of aldrin or dieldrin showed no ill-effects during the 2 years of the study. In the dogs fed aldrin at 1.0 mg/kg/day or dieldrin at 0.5 mg/kg/day, fatty degeneration was observed in the liver and kidneys. This study also was too short-termed to determine tumorigenic properties of aldrin and dieldrin. The number of animals surviving at the end of the study was inadequate to make any type of evaluation.

A third short-termed study on dieldrin in dogs was carried out by Walker, et al. (1969). Dieldrin (99+ percent purity) was administered to groups of five male and five female dogs in gelatine capsules at 0.005 and 0.05 mg/kg/day. After two years, the health and body weight of the treated dogs, as compared to the controls, was normal. A variety of physiological tests confirmed the general good health of the dogs. In dogs administered the higher concentration of dieldrin, liver-to-body weight ratios were increased significantly over the controls. The report stated that no lesions were seen in the tissues but provided no data on this.

There has been one report on the effects of dieldrin on Rhesus monkeys. The unpublished work of Zavon and Stemmer (1975), from the Kettering Laboratory, reports on a study in which six control monkeys (five male, one female) and groups of five monkeys received 0, 0.01, 0.1, 0.5, 1.0 or 1.75 mg/kg dieldrin in their diet for 5.5 to 6 years. The group at 1.75 mg/kg received 5.0 mg/kg for four months, then 2.5 mg/kg for approximately 2.5 months, and then 1.75 mg/kg for the remainder of the exposure. Additionally, one monkey in this group had its dieldrin intake progressively increased to the 5 mg/kg concentration. The authors state that this animal and three others died during the study. These animals had received 5.0, 1.0 or 0.1 mg/kg dieldrin in their diets. The remaining animals survived until they were killed.

Fat biopsies were taken on selected animals at various intervals. Dieldrin blood levels and other parameters were determined throughout the study.

The authors concluded that there were no significant hepatic changes other than alterations in cytochrome P-450 levels. They also stated that there was no indication of dieldrin-associated malignancies although admittedly this was not considered a cancer study. It was also the opinion of the authors that the premature deaths were not related to the ingestion of dieldrin.

Versteeg and Jager (1973) summarized health studies carried out on pesticide workers in the Shell plant in Holland. These workers had occupational exposure to aldrin/dieldrin over periods of up to 12.3 years with a mean of 6.6 years. The average time that had elapsed from the end of exposure was 7.4 years (maximum, 16 years). The average age of the group was 47.4 years. The report states that 233 long-term workers were involved in this study and that no permanent adverse effects (including cancer) on the workers' health were observed.

Recently, Van Raalte (1977) published a follow-up on presumably the same group of workers reported on by Versteeg and Jager (1973). This study listed the various physiological parameters which were examined in workers with more than four years of exposure. These workers were examined in terms of two categories, one having workers with more than four years exposure and more than 15 years of observation (a total of 166 men) and the other with more than ten years exposure and more than 15 years of observation (69 men). While this is the same number of subjects in both studies done at the same plant, Versteeg and Jager listed aldrin/dieldrin and other pesticide exposures while Van Raalte only mentioned dieldrin. This study appears to be a continuation of the previously reported work with an additional number of years of exposure and observation. The author states that again there were no persisting medical problems in the workers and no increase in cancer. Van Raalte also goes on to point out that several other of the human carcinogens have been detected in limited populations after relatively short times. He suggests that the lack of early adverse health signs and the lack of an increase in cancer at this time strengthens the assumption that dieldrin is not a human carcinogen.

While it is most likely correct to assume that these workers are probably the most highly exposed group available for study, the total number is again rather small and the observation times are still less than 20 years.

Epstein (1975a) states that the epidemiological aspects of the study carried out by Shell have been reviewed by several experts who have criticized the study as inadequate due to the number of workers at risk and the short duration of exposure and/or time after exposure.

CRITERION FORMULATION

Existing Guidelines and Standards

Prior to 1974, aldrin and dieldrin were approved for use on 46 agricultural crops and for treatment of soil around fruits, grains, nuts, and vegetables (Int. Agency Res. Cancer, 1974a,b). In 1974 the registration of aldrin and dieldrin was suspended on the basis of adverse health affects in rodents (39 FR 37251). As a result, production is restricted for all pesticide products containing aldrin or dieldrin. Aldrin and dieldrin can no longer be used for spraying and dusting, or for mothproofing in which the residues are discharged into waterways. All uses in structures occupied by humans or livestock, uses upon turf, and any use involving application to any aquatic environment are also restricted. Aldrin and dieldrin can be used for termite treatment which involves direct application to the soil and therefore little movement of the pesticides. They may also be used for treatment of some nonfood seeds and plant dipping during transplantation.

The current exposure level for both aldrin and dieldrin set by the Occupational Safety and Health Administration is an air time-weighted average (TWA) of 250 $\mu g/m^3$ for skin absorption (37 FR 22139). In 1969, the U.S. Public Health Service Advisory Committee recommended that the drinking water standards for both aldrin and dieldrin be 17 $\mu g/l$ (Mrak, 1969). Also, the U.N. Food and Agriculture Organization/World Health Organization's acceptable daily intake for aldrin and dieldrin is 0.0001 mg/kg/day (Mrak, 1969).

Current Levels of Exposure

The people of the United States are exposed to aldrin and dieldrin in air, water, and food. As mentioned earlier, aldrin or dieldrin has been found in more than 85 percent of the air samples tested by the U.S. EPA (Epstein, 1976). The levels were as high as 2.8 ng/m^3 resulting in an intake of up to 0.098 µg/day. Dieldrin can travel great distances in the air, especially when absorbed to particulate matter. Thus people can potentially be exposed to pesticide treatments from other countries.

Waters recently sampled in the United States contained aldrin or dieldrin in amounts up to 0.05 µg/l (Harris, et al. 1977). The standard diet in the United States has been calculated to contain approximately 43 ng/g of dieldrin. According to Epstein (1976) tolerances for dieldrin in cattle-meat fat, milk fat, meat, and meat by-products have been petitioned for at levels of 0.3, 0.2, and 0.1 ppm, respectively.

Special Groups at Risk

Children, especially infants, have a high dairy product diet that has been shown to contain dieldrin (Manske and Johnson, 1975). It has also been demonstrated that human milk contains dieldrin residues and that some infants may be exposed to high concentrations of dieldrin from that source alone (Savage, 1976).

In early studies, Curley and Kimbrough (1969) and Zavon, et al. (1969) reported that dieldrin and several other chlorinated hydrocarbon pesticides were present in the tissues of stillborn infants. Curley, et al. (1969) also reported that dieldrin and other pesticides could be found in the blood of newborn infants.

No work has been carried out on neonatal animals with either aldrin or dieldrin; however, due to the sensitivity of neonatal animals to other carcinogens, this should be an area of great concern.

Basis and Derivation of Criteria

The aldrin and dieldrin carcinogenicity data of Walker, et al. (1972) and the National Cancer Institute (1976) (43 FR 2450) were analyzed using a linearized multistage model as discussed in the Human Health Methodology Appendices to the October 1980 Federal Register notice which announced the availability of this document. It should be noted that the Walker, et al. study used 99 percent pure dieldrin while the NCI study used technical grade dieldrin.

Under the Consent Decree in NRDC v. Train, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." Both aldrin and dieldrin are suspected of being human carcinogens. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of aldrin/dieldrin in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and states in the possible future development of water quality regulations, the concentrations of aldrin and dieldrin corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5}

for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the Federal Register notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, 10^{-6} or 10^{-7} as shown in the table below.

Exposure Assumptions	Risk Levels and Corresponding Criteria(1)			
	0 ng/l	10^{-7} ng/l	10^{-6} ng/l	10^{-5} ng/l
2 liters of drinking water and consumption of 6.5 grams of fish and shellfish (2)				
Aldrin	0	0.0074	0.074	0.74
Dieldrin	0	0.0071	0.071	0.71
Consumption of fish and shellfish only.				
Aldrin	0	0.0079	0.079	0.79
Dieldrin	0	0.0076	0.076	0.76

(1) Calculated by applying a linearized multistage model as discussed above. Appropriate bioassay data used in the calculation of the model are presented in Appendix I. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

(2) Ninety-four percent of aldrin exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 28-fold, but for purposes of criterion development are assumed to bioconcentrate aldrin at 4670, because aldrin is converted to, and stored as dieldrin in these organisms (see Appendix I). The remaining 6 percent of aldrin exposure results from drinking water.

Ninety-four percent of dieldrin exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 4670-fold. The remaining 6 percent of dieldrin exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of aldrin/dieldrin, (1) occurring from the consumption of both drinking water and aquatic life grown in water containing the corresponding aldrin/dieldrin concentrations and, (2) occurring solely from the consumption of aquatic life grown in the waters containing the corresponding aldrin/dieldrin concentrations.

Although total exposure information for aldrin and dieldrin is discussed and an estimate of the contributions from other sources of exposure can be made, this data will not be factored into the ambient water quality criteria formulation because of the tenuous estimates. The criteria presented, therefore, assume an incremental risk from ambient water exposure only.

REFERENCES

Ahmed, F.E., et al. 1977a. Pesticide-induced DNA damage and its repair in cultured human cells. Mutat. Res. 42: 161.

Ahmed, F.E., et al. 1977b. Pesticide-induced ouabain resistant mutants in Chinese hamster V79 cells. Chem. Biol. Interactions. 19: 369.

Ames, B.N., et al. 1975. Methods for detecting carcinogens and mutagens with the *Salmonella*/Mammalian-Microsome Mutagenicity test. Mutat. Res. 31: 347.

Baldwin, M.K., et al. 1972. A comparison of the metabolism of HEOD (dieldrin) in the CFl mouse with that in the CFE rat. Food Cosmet. Toxicol. 10: 333.

Barnes, J.M. and D.R. Heath. 1964. Some toxic effects of dieldrin in rats. Br. Jour. Ind. Med. 21: 280.

Barron, R.L. and M.S. Walton. 1971. Dynamics of HEOD (dieldrin) in adipose tissue of the rat. Toxicol. Appl. Pharmacol. 18: 958.

Bedford, C.T. and D.H. Hutson. 1976. The comparative metabolism in rodents of the isomeric insecticides dieldrin and endrin. Chem. Ind. 10: 440.

Bidwell, K., et al. 1975. Comprehensive evaluation for mutagenic activity of dieldrin. Mutat. Res. 31: 314.

Bunch, T. and J.R. Low. 1973. Effects of dieldrin on chromosomes of semi-domestic mallard ducks. Jour. Wildl. Manage. 37: 51.

Burchfiel, J.L., et al. 1976. Persistent effects of sarin and dieldrin upon primate electroencephalogram. Toxicol. Appl. Pharmacol. 35: 365.

Cabral, J.R.P., et al. 1979. A carcinogenicity study of the pesticide dieldrin in hamsters. Cancer Lett. 6: 241.

Chernoff, N., et al. 1975. Prenatal effects of dieldrin and photodieldrin in mice and rats. Toxicol. Appl. Pharmacol. 31: 302.

Clark, C.R. and R.I. Krieger. 1976. Beta-diethylaminoethyl-diphenylpropylacetate (SKF 525-A) enhancement of tissue accumulation of aldrin in mice. Toxicol. Appl. Pharmacol. 38: 315.

Cleveland, F.P. 1966. A summary of work on aldrin and dieldrin toxicity at the Kettering Laboratory. Arch. Environ. Health. 13: 195.

Cole, J.F., et al. 1970. Endrin and dieldrin: A comparison of hepatic excretion in the rats. Toxicol. Appl. Pharmacol. 16: 547.

Cueto, C., Jr. and F.J. Biros. 1967. Chlorinated insecticides and related materials in human urine. Toxicol. Appl. Pharmacol. 10: 261.

Cueto, C., Jr. and W.J. Hayes, Jr. 1962. The detection of dieldrin metabolites in human urine. Jour. Agric. Food Chem. 10: 366.

Curley, A. and R. Kimbrough. 1969. Chlorinated hydrocarbon insecticides in plasma and milk of pregnant and lactating women. Arch. Environ. Health. 18: 156.

Curley, A., et. al. 1969. Chlorinated hydrocarbon insecticides in organs of stillborn and blood of newborn babies. Arch. Environ. Health. 19: 628.

Dale, W.E. and G.E. Quinby. 1963. Chlorinated insecticides in the body fat of people in the United States. Science. 142: 593.

Davis, K.J. 1965. Pathology report on mice for aldrin, dieldrin, heptachlor, or heptachlor epoxide for two years. Int. Food and Drug Admin.

Davis, K.J. and O.G. Fitzhugh. 1962. Tumorigenic potential of aldrin and dieldrin for mice. Toxicol. Appl. Pharmacol. 4: 187.

Dean, B.J., et al. 1975. The potential mutagenicity of dieldrin (HEOD) in mammals. Food Cosmet. Toxicol. 13: 317.

Deichmann, W.B. 1972. Toxicology of DDT and related chlorinated hydrocarbon pesticides. Jour. Occup. Med. 14: 285.

Deichmann, W.B., et al. 1967. Synergism among oral carcinogens in the simultaneous feeding of four tumorigens to rats. Toxicol. Appl. Pharmacol. 11: 88.

Deichmann, W.B., et al. 1968. Retention of dieldrin in blood, liver, and fat of rats fed dieldrin for six months. Ind. Med. Surg. 37: 837.

Deichmann, W.B., et al. 1969. Retention of dieldrin and DDT in the tissues of dogs fed aldrin and DDT individually and as a mixture. Toxicol. Appl. Pharmacol. 14: 205.

Deichmann, W.B., et al. 1970. Tumorigenicity of aldrin, dieldrin and endrin in the albino rat. Ind. Med. Surg. 39: 426.

Dix, K.M., et al. 1977. Toxicity studies with dieldrin: Teratological studies in mice dosed orally with HEOD. Teratology. 16: 57.

Domanski, J.J., et al. 1977. Relation between smoking and levels of DDT and dieldrin in human fat. Arch. Environ. Health. 32: 196.

Edwards, C.A. 1973. Persistent Pesticides in the Environment. CRC Press, Inc., Cleveland, Ohio.

Eliason, B.C. and H.S. Posner. 1971a. Reduced passage of carbon-14-dieldrin to the fetal rat by phenobarbital but not by eight other drugs or dieldrin. Am. Jour. Obstet. Gynecol. 110: 943.

Eliason, B.C. and H.S. Posner. 1971b. Placental passage of ^{14}C-dieldrin altered by gestational age and plasma proteins. Am. Jour. Obstet. Gynecol. 111: 925.

Epstein, S.S. 1975a. The carcinogenicity of dieldrin. Part I. Sci. Total Environ. 4: 1.

Epstein, S.S. 1975b. The carcinogenicity of dieldrin. Part II. Sci. Total Environ. 4: 205.

Epstein, S.S. 1976. Case study 5: Aldrin and dieldrin suspension based on experimental evidence and evaluation and societal need. Ann. N.Y. Acad. Sci. 271: 187.

Fahrig, R. 1973. Comparative mutagenicity studies with pesticides. Chem. Carcinogenesis Essays. 10: 161.

Feil, V.J., et al. 1970. Dieldrin-^{14}C metabolism in sheep. Jour. Agric. Food Chem. 18: 120.

Fitzhugh, O.G., et al. 1964. Chronic oral toxicity of aldrin and dieldrin in rats and dogs. Food Cosmet. Toxicol. 2: 551.

Gunther, R.A., et al. 1968. Reported solubilities in 738 pesticide chemicals in water. Residue Rev. 20: 1.

Hansch, C. and J. Leo. 1979. Substituent Constants for Correlation Analysis in Chemistry and Biology. Wiley Interscience, New York.

Harris, R.H., et al. 1977. Carcinogenic Hazards of Organic Chemicals in Drinking Water. In: H.H. Hiatt, et al. (eds.) Origins of Human Cancer. Cold Spring Harbor Lab., New York. p. 309.

Hathaway, D.E., et al. 1967. Transport of dieldrin from mother to blastocyst and from mother to foetus in pregnant rabbits. Eur. Jour. Pharmacol. 1: 167.

Hayes, W.J. 1971. Toxicology of Pesticides. The Williams and Wilkins Co., Baltimore, Maryland.

Hayes, W.J. 1974. Distribution of dieldrin following a single oral dose. Toxicol. Appl. Pharmacol. 28: 485.

Hayes, W.J. and A. Curley. 1968. Storage and excretion of dieldrin and related compounds: Effect of occupational exposure. Arch. Environ. Health. 16: 155.

Heath, D.F. and M. Vandekar. 1964. Toxicity and metabolism of dieldrin in rats. Br. Jour. Ind. Med. 21: 269.

Hedde, R.D., et al. 1970. Dieldrin-^{14}C metabolism in sheep distribution and isolation of urinary metabolites. Jour. Agric. Food Chem. 18: 116.

Hodge, H.C., et al. 1967. Toxicology and no-effect levels of aldrin and dieldrin. Toxicol. Appl. Pharmacol. 10: 613.

Hoogendam, I., et al. 1962. Electroencephalograms in insecticide toxicity. Arch. Env. Health. 4: 92.

Hootsman, W.J.M. 1962. Deklinische belekenis van net electroencephalogram. Ned. T. Geneesk. 106: 2584.

Hunter, C.G., et al. 1969. Pharmacodynamics of dieldrin (HEOD). Arch. Environ. Health. 18: 12.

International Agency for Research on Cancer. 1974a. Evaluation of carcinogenic risk: Aldrin. IARC Monogr. 5: 25.

International Agency for Research on Cancer. 1974b. Evaluation of carcinogenic risk: Dieldrin. IARC Monogr. 5: 125.

Jager, K.W. 1970. Aldrin, Dieldrin, Endrin and Telodrin: An Epidemiological and Toxicological Study of Long-term Occupational Exposure. Elsevier Publishing Co., Amsterdam.

Keane, W.T., et al. 1969. Dieldrin poisoning in dogs: Relation to obesity and treatment. Brit. Jour. Ind. Med. 26: 338.

Klein, A.K., et al. 1968. Isolation and purification of metabolites found in the urine of male rats fed aldrin and dieldrin. Jour. Assoc. Off. Chem. 51: 895.

Kohli, K.K., et al. 1977. Induction of mixed function oxidases on oral administration of dieldrin. Chem. Boil. Interactions. 17: 249.

Korte, F. 1963. Metabolism studies with C^{14}-labelled insecticides. Fifth Int. Pestic. Congr., London.

Korte, F. and H. Arent. 1965. Metabolism of insecticides. IX (1) Isolation and identification of dieldrin metabolites from urine of rabbits after oral administration of dieldrin-^{14}C. Life Sci. 4: 2017.

Ludwig, G., et al. 1964. Excretion and distribution of aldrin-^{14}C and its metabolites after oral administration for a long period of time. Life Sci. 3: 123.

MacKay, D. and A.W. Wolkoff. 1973. Rate of evaporation of low-solubility contaminants from water bodies to atmosphere. Environ. Sci. Technol. 7: 611.

Majumdar, S.K., et al. 1976. Dieldrin-induced chromosome damage in mouse bone-marrow and WI-38 human lung cells. Jour. Hered. 67: 303.

Majumdar, S.K., et al. 1977. Mutagenicity of dieldrin in the *Salmonella*/microsome test. Jour. Hered. 68: 194.

Manske, D.D. and R.D. Johnson. 1975. Pesticide residues in total diet samples (VIII). Pestic. Monitor. Jour. 9: 94.

Marigold, D.B. and J.A. Schulze. 1969. Pesticides in water: Pesticides in selected western streams - A progress report. Pestic. Monitor. Jour. 3: 124.

Markaryan, D.S. 1966. Cytogenetic effect of some chlororganic insecticides on mouse bone-marrow cell nuclei. Genetika. 2: 132.

Marshall, T.C., et al. 1976. Screening of pesticides for mutagenic potential using *Salmonella typhimurium* mutants. Jour. Agric. Food Chem. 24: 560.

Matsumura, F. 1974. Toxicology of Insecticides. Plenum Press, New York.

Matsumura, F. and G.M. Boush. 1967. Dieldrin: Degradation by soil microorganisms. Science. 156: 959.

Matthews, H.B. and F. Matsumura. 1969. Metabolic fate of dieldrin in the rat. Jour. Agric. Food Chem. 17: 845.

Matthews, H.B., et al. 1971. Dieldrin metabolism, excretion, and storage in male and female rats. Jour. Agric. Food Chem. 19: 1244.

Mick, D.L., et al. 1971. Aldrin and dieldrin in human blood components. Arch. Environ. Health. 23: 177.

Mrak, E.M. 1969. Chairman 1969 report of the secretary's commission on pesticides and their relationship to environment health. U.S. Dept. Health, Edu. Welfare, Washington, D.C.

Nakatsugawa, T., et al. 1965. Microsomal expoxidation of cyclodiene insecticides. Biochem. Pharmacol. 14: 1853.

Nash, R.G. and E.A. Woolson. 1967. Persistence of chlorinated hydrocarbon insecticides in soils. Science. 157: 924.

National Academy of Sciences, National Research Council. 1975. Pest control: An assessment of present and alternative technologies. Vol. 1. Contemporary pest control practices and prospects. Natl. Acad. Sci., Washington, D.C.

Ottolenghi, A.D., et al. 1974. Teratogenic effects of aldrin, dieldrin and endrin in hamsters and mice. Teratology. 9: 11.

Park, K.S. and W.N. Bruce. 1968. The determination of the water solubility of aldrin, dieldrin, heptachlor and heptachlor epoxide. Jour. Econ. Entomol. 6: 770.

Parrish, P.R. 1974. Arochlor 1254, DDT and DDD, and dieldrin: accumulation and loss by American oysters (Crassostrea virginica) exposed continuously for 56 weeks. Proc. Natl. Shellfish. Assoc. 64: 7.

Radomski, J.L. and B. Davidow. 1953. The metabolite of heptachlor, its estimation, storage and toxicity. Jour. Pharmacol. Exp. Ther. 107: 266.

Reinert, R.E., et al. 1974. Dieldrin and DDT: Accumulation from water and food by lake trout (Salvelinus namaycush) in the laboratory. Proc. 17th Conf. Great Lakes Res. 52.

Richardson, A., et al. 1968. Metabolites of dieldrin (HEOD) in the urine and feces of rats. Chem. Ind. 18: 588.

Robinson, J., et al. 1969. The pharmacokinetics of HEOD (dieldrin) in the rat. Food Cosmet. Toxicol. 7: 317.

Savage, E.P. 1976. National study to determine levels of chlorinated hydrocarbon insecticides in human milk: 1975-1976 and supplementary report to national human milk study: 1975-1976. EPA/540/9-78/005. NTIS, Springfield, Virginia. PB 284393.

Scholes, M.E. 1955. The effects of aldrin, dieldrin, isodrin, endrin and DDT on mitosis in roots of the onion (allium cepal). Jour. Hort. Sci. 30: 181.

Shannon, L.R. 1977a. Accumulation and elimination of dieldrin in muscle tissue of channel catfish. Bull. Environ. Contam. Toxicol. 17: 637.

Shannon, L.R. 1977b. Equilibrium between uptake and elimination of dieldrin by channel catfish, Ictalurus punctatus. Bull. Environ. Contam. Toxicol. 17: 178.

Shirasu, Y., et al. 1977. Mutagenicity Screening on Pesticides and Modification Products: A Basis of Carcinogenicity Evaluation. In: H.H. Hiatt, et al. (eds.) Origins of Human Cancer. Cold Spring Harbor Lab., New York. p. 267.

Skalsky, H.L. and F.E. Guthrie. 1978. Binding of insecticides to human serum proteins. Toxicol. Appl. Pharmacol. 43: 229.

Soto, A.R. and W.B. Deichmann. 1967. Major metabolism and acute toxicity of aldrin, dieldrin and endrin. Environ. Res. 1: 307.

Stanley, C.W., et al. 1971. Measurement of atmospheric levels of pesticides. Environ. Sci. Technol. 5: 430.

Stephan, C.E. 1980. Memorandum to J. Stara. U.S. EPA. July 3.

Street, J.C. 1964. DDT antagonism to dieldrin storage in adipose tissue. Science. 146: 1580.

Street, J.C. and A.D. Blau. 1966. Insecticide interactions affecting residue accumulation in animal tissues. Toxicol. Appl. Pharmacol. 8: 497.

Thorpe, E. and A.I.T. Walker. 1973. The toxicology of dieldrin (HEOD). Part II. Comparative long-term oral toxicity studies in mice with dieldrin, DDT, phenobarbitone, beta-BHC and gamma-BHC. Food Cosmet. Toxicol. 11: 433.

Treon, J. and F.D. Cleveland. 1955. Toxicity of certain chlorinated hydrocarbon insecticides for laboratory animals with special reference to aldrin and dieldrin. Agric. Food Chem. Jour. 3: 402.

U.S. Department of Agriculture. 1966. The Pesticide Review. Agric. Stabili. Conserv. Serv., Washington, D.C.

U.S. EPA. 1971. Reasons underlying the registration decision concerning products containing DDT, 2,4,5-T, aldrin and dieldrin.

U.S. EPA. 1976. National interim primary drinking water regulations. Publ. No. 570/9-76-003.

U.S. EPA. 1980. Seafood consumption data analysis. Stanford Research Institute International. Menlo Park, California. Final Report, Task 11, Contract No. 68-01-3887.

Van Raalte, H.G.S. 1977. Human experience with dieldrin in perspective. Ecotox. Environ. Safety. 1: 203.

Veith, G.D., et al. 1979. Measuring and estimating the bioconcentration factor of chemicals in fish. Jour. Fish Res. Board. Can. 36: 1040.

Veith, G.D. 1980. Memorandum to C.E. Stephan. U.S. EPA. April 14.

Versteeg, J.P.J. and K.W. Jager. 1973. Long-term occupational exposure to the insecticides aldrin, dieldrin, endrin, and telodrin. Br. Jour. Ind. Med. 30: 201.

Wade, M.J., et al. 1979. Mutagenic action of a series of epoxides. Mutat. Res. 66: 367.

Walker, A.I.T., et al. 1969. The toxicology and pharmacodynamics of dieldrin (HEOD): Two-year oral exposures of rats and dogs. Toxicol. Appl. Pharmacol. 15: 345.

Walker, A.I.T., et al. 1972. The toxicology of dieldrin (HEOD). Long-term oral toxicity studies in mice. Food Cosmet. Toxicol. 11: 415.

Weaver, L., et al. 1965. Chlorinated hydrocarbon pesticides in major U.S. River basins. Public Health Rep. 80: 481.

Winteringham, F.P.W. and J.M. Barnes. 1955. Comparative response of insects and mammals to certain halogenated hydrocarbons used as pesticides. Physiol. Rev. 35: 701.

Wolfe, H.R., et al. 1972. Exposure of spraymen to pesticides. Arch. Environ. Health. 25: 29.

Wong, D.T. and L.C. Terriere. 1965. Epoxidation of aldrin, isodrin, and heptachlor by rat liver microsomes. Biochem. Pharmacol. 14: 375.

Wurster, C.F. 1971. Aldrin and dieldrin. Environ. 13: 33.

Zavon, M.R. and K.L. Stemmer. 1975. The effect of dieldrin ingestion in Rhesus monkeys: A six-year study. Unpublished report from the Kettering Laboratory, University of Cincinnati, Cincinnati, Ohio.

Zavon, M.R., et al. 1969. Chlorinated hydrocarbon pesticide content of the neonate. Ann. N.Y. Acad. Sci. 160: 1969.

APPENDIX 1

Summary and Conclusions Regarding the Carcinogenicity of Aldrin and Dieldrin*

Aldrin has induced liver tumors in males and females of three strains of mice according to reports of four separate chronic feeding studies. It has failed to induce a statistically significant carcinogenic response in rats at any site according to reports of five studies in two different strains. In two bacterial assays with and without activation (*S. typhimurium* and *E. coli*) it was found to be nonmutagenic, but it did produce unscheduled DNA synthesis in human fibroblasts with and without activation. The induction of hepatocellular carcinoma in both male and female mice from the administration of aldrin leads to the conclusion that it is likely to be a human carcinogen.

Dieldrin, which is readily formed from aldrin in the environment and by metabolism of aldrin in rats, mice, fish, and many other species, has produced liver tumors in four strains of mice according to six reports of chronic feeding studies and possible liver tumors in an unpublished study with a fifth strain. In rats it has failed to induce a statistically significant excess of tumors at any site in six chronic feeding studies in three strains. It was found to be mutagenic in *S. typhimurium* after metabolic activation with mouse liver enzymes, but it was not mutagenic in two other studies of the same bacterial strain with a rat liver enzyme activation mixture. The induction of hepatocellular carcinomas in mice leads to the conclusion that dieldrin is likely to be a human carcinogen.

---

*This summary has been prepared and approved by the Carcinogens Assessment Group, U.S. EPA, on July 25, 1979.

Both aldrin and dieldrin have been found to be nonmutagenic in several test systems as follows: a) gene conversion in _S. cerevisie_; b) back mutations in _S. marcescens_, and c) foward mutations at two loci in _E. coli_. Several other organochlorine pesticides which produce mouse liver tumors are also nonmutagenic in the same systems.

The induction of liver tumors in mice of both sexes by aldrin and dieldrin is sufficient evidence that they are likely to be human carcinogens.

The water quality criterion for aldrin is based on the hepatocellular carcinoma incidence in male B6C3F1 mice in the NCI chronic test, and on this same response in groups of female CF-1 mice in the Walker, et al. (1972) experiment, because aldrin is converted to and stored as dieldrin in fish. It is concluded that the water concentration of aldrin should be less than 0.74 ng/l in order to keep the lifetime cancer risk below 10^{-5}. For dieldrin the criterion is based on the response in groups of female CF-1 mice in the Walker, et al. (1972) experiment. The corresponding concentration for dieldrin is 0.71 ng/l.

Summary of Pertinent Data for Aldrin

The water quality criterion for aldrin is derived from the hepatocellular carcinoma response of the B6C3F1 male mice given aldrin in the NCI bioassay test. The slope of the one-hit dose-response curve for aldrin is calculated from the following parameters:

Dose (mg/kg/day)	Incidence (no. responding/no. tested)
0.0	3/30
0.52	16/49
1.04	25/46

le = 80 weeks　　w = 0.035 kg

Le = 90 weeks

L = 90 weeks

With these parameters the carcinogenic potency factor for humans, q_1^*, for aldrin is 11.45 $(mg/kg/day)^{-1}$.

The conversion of aldrin to dieldrin in fish results in the accumulation of dieldrin residues in fish exposed to aldrin. This makes it necessary to consider the risk resulting from intake of dieldrin stored in fish due to the presence of aldrin in water. Thus, the criterion for aldrin also depends upon the carcinogenic potency factor for humans, q_1^*, for dieldrin, which is 30.37 $(mg/kg/day)^{-1}$.

The equation describing the risk due to aldrin in water is derived from the general relationship:

$P = B_H D$ and $D = I/70$ kg, thus

$P = B_H\ I/70$ kg and

$P(70\ \text{kg}) = B_H I$

where

P = individual lifetime risk (set at 10^{-5} for criterion calculation)

I = average daily human intake of the substance in question

B_H = estimated carcinogenic potency factor for humans

70 kg = average weight of humans

Since aldrin in water leads to the accumulation of dieldrin residues in fish, the equation describing the risk due to aldrin is:

$$Pa\ (70\ \text{kg}) = B_{Ha}\ C_a\ (2.0\ \text{l/day}) + B_{Ha}\ C_a\ R_{ad}\ (0.0065\ \text{kg/day}) + B_{Hd}\ C_a\ R_{ad}\ (0.0065\ \text{kg/day})$$

where

P_a = risk due to aldrin (set at 10^{-5} for criterion calculation)

B_{Ha} = 11.45 $(\text{mg/kg/day})^{-1}$, the aldrin carcinogenic potency factor for humans

B_{Hd} = 30.37 $(\text{mg/kg/day})^{-1}$, the dieldrin carcinogenic potency factor for humans

C_a = criterion concentration for aldrin (to be calculated)

R_a = 28 l/kg, the fish bioconcentration of aldrin from aldrin

R_{ad} = 4642 l/kg, the fish bioconcentration of dieldrin from aldrin

2.0 l/day = average daily intake of water for humans

0.0065 kg/day = average daily intake of fish for humans

The term containing R_{ad} represents intake of dieldrin resulting from the presence of aldrin in the water, and is thus multiplied by the dieldrin dose-response slope. R_{ad} is estimated by assuming that in the absence of conversion to dieldrin, aldrin would bioconcentrate 4670 times (as dieldrin does), and that since aldrin only accumulates 28 times, the remainder of the expected aldrin residues are being stored as dieldrin (i.e., 4670 - 28 = 4642).

The result is that the water concentration of aldrin should be less than 0.74 ng/l in order to keep the individual lifetime risk below 10^{-5}.

Summary of Pertinent Data for Dieldrin

The water quality criterion for dieldrin is based on the hepatocellular carcinoma response of the female CF-1 mice given various concentrations of dieldrin continuously in the diet in the experiment of Walker, et al. (1972). The parameters of the dose-response model are:

Dose (mg/kg/day)[1]	Incidence (no. responding/no. tested)
0.0013	39/297
0.013	24/90
0.128	32/87
1.28	136/148

le = 924 days

Le = 924 days

L = 924 days

w = 0.030 kg

R = 4670 l/kg

With these parameters the carcinogenic potency factor for humans, q_1^*, is 30.37 $(mg/kg/day)^{-1}$. The result is that the water concentration should be less than 0.71 ng/l in order to keep the individual lifetime risk below 10^{-5}.

---

[1] Doses are concentrations determined to be in the diet. The first dose group, the control, was found to have a level of contamination in the diet equivalent to 0.0013 mg/kg/day.